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Dietary supplements for mood improvement and stress relief: producers' and merchants' declarations vs state of knowledge

Aleksandra Brzozowska, Jakub Grabowski, Aleksandra Grzyb

Abstract

The market for dietary supplements intended to improve mood or reduce negative effects of stress is of considerable size (estimated at $656 mln globally in 2022). In the UE 10% of people who consume dietary supplements, do it to reduce depression, stress or anxiety. The statistics are higher for women and people aged 18-44. In Poland specifically, out of 89% of adults who used dietary supplements or OTC medications in the previous year 13% chose products that affect mental health in some way. Popularity of such preparations may reflect higher prevalence of psychological distress, low availability of professional mental healthcare (i.e. psychiatrists, psychologists and psychotherapists) as well as social stigma of receiving professional treatment for mental disorders. The aim of this review was to present the current state of knowledge about the most popular herbal ingredients included in preparations advertised as mood enhancers or stress relievers. An internet search was performed to identify 10 most popular herbal ingredients found in this kind of products and collect producers'/merchants' declarations as to the expected results. For each ingredient research was performed using PubMed, Google Scholar, Cochrane Library and Up to Date to present evidence-based-knowledge relating to mood and stress. The main conclusion is that herbs are widely used in preparations addressing psychological distress and herbal ingredients used in the mental health sector need to be thoroughly researched, both in terms of psychopharmacology and public health to identify potentially hazardous patterns of consumption and introduce proper education, if needed.

mental healthcare; depressive disorder; anxiety disorders; dietary supplements; stress

1. INTRODUCTION

The market for dietary supplements addressing the problem of depressed mood or negative effects of stress has grown to a considerable degree in the recent years, with category growth reaching 62% in 2022 in comparison with 2018 in the USA [1]. Globally, its estimated value in 2022 was $656 million and is predicted to reach $1.3 billion in 2033, assuming projected annual growth rate of 6.4% [2]. On the European market for dietary supplements affecting mental and cognitive functions, there is domination of herbal products (42.9%) [3]. They are easily accessible both online and in stationary pharmacies, drugstores, herbal stores and even supermarkets.

In terms of general psychopathology, a depressed mood is defined as subjective feeling

Aleksandra Brzozowska[1], Jakub Grabowski[2], Aleksandra Grzyb[1]: [1] Adult Psychiatry Scientific Circle, Division of Developmental Psychiatry, Psychotic and Geriatric Disorders, Department of Psychiatry, Faculty of Medicine, Medical University of Gdansk; [2] Division of Developmental Psychiatry, Psychotic and Geriatric Disorders, Department of Psychiatry, Faculty of Medicine, Medical University of Gdansk

Correspondence address: abrzozowska@gumed.edu.pl

of sadness, grief, hopelessness or indifference and is often accompanied by anxiety, low self-esteem, pessimistic attitude towards future and suicidal thoughts [4]. If certain diagnostic criteria are met, diagnoses of major depressive disorder or persistent depressive disorder (dysthymia) may be made [5]. Experiencing a short-lived depressed mood, i.e. a state that does not fulfil criteria of any mood disorder, is common among apparently healthy individuals and despite its rather mild character, it may still be a reason for suffering and decreased life quality [6-9].

In terms of the most traditional definition, "Stress is a non-specific response of the body to any demand" [10]. It is of considerable value to look at stress reactions from the transactional point of view, that is to see stress as a specific relationship between an individual and the surroundings that is assessed by the individual as taxing, dangerous or exceeding their capabilities [11]. The list of events that may cause stress in people is inexhaustible and includes not only the objectively negative ones (e.g. death of a relative, divorce, personal injury, illness, getting fired at work, trouble with boss, taking a loan) but also events with positive context (e.g. vacation, promotion at work, outstanding personal achievement) [12,13]. In response to stressful events individuals may experience certain negative symptoms both at psychological and biological level. Common stress-related difficulties include emotional lability, irritability, impaired concentration, impaired memory, loss of appetite, sleep disturbances, gastrointestinal problems, increased muscle tone, headaches, increased BP and HR, cardiac arrhythmias, coronary heart disease, atherosclerosis, hypertension and chronic inflammation, just to name a few [14,15]. Corticosteroids, catecholamines, vasoactive intestinal peptide, vasopressin, somatostatin are some of the hormones involved in stress reactions at the molecular level, with hypercortisolaemia being linked to chronic stress [16-18].

2. THE MARKET FOR PREPARATIONS INTENDED TO IMPROVE MOOD OR REDUCE THE EFFECTS OF STRESS IN POLAND

The market for dietary supplements is on the rise in Poland with estimated value of $1.1billion in 2019 [19] and $1.92 billion in 2022 [20]. The statistics concerning consumption of dietary supplements in Poland vary but are considerable. Consumer survey on food supplements in the UE [21] reports that 88% of adult EU inhabitants have ever used a dietary supplement in their lives, with figures being higher in the Eastern Europe. In Poland specifically, 93% of those who have ever used dietary supplements, have used them in the recent year and the mean number of dietary supplements used per year was 4. According to CBOS [22], 89% of adult Poles use over-the-counter medications or dietary supplements, a considerable proportion of which use some preparations affecting psychological functioning (anxiolytic and sleep preparations – 13%, memory and concentration preparations – 10%).

In order to identify herbal ingredients included in dietary supplements available on the Polish market, an Internet search was performed in March 2024. Phrases such as "preparaty na poprawę nastroju" ("preparations for mood improvement") and "preparaty na stres" ("preparations for stress") were introduced into Google search engine. For each phrase 50 first results were taken into consideration. Repeated preparations, products there were not dietary supplements (i.e. drugs or medical devices) and preparations not containing herbal ingredients were excluded. Only preparations for adults were taken into consideration. Table 1 presents lists of herbal ingredients in preparations sold in each indication.

Table 1. Lists of herbal ingredients contained in preparations for mood improvement or stress relief available on the Polish market.

Preparations for mood improvement	Preparations for stress
– Hypericum perforatum extract (St. John's wort) – Crocus sattivus (saffron) flower extract – Melissa officinalis extract – Crateugus (hawthorn) fruit extract – Lavandula sp. extract – Withania somnifera (ashwagandha) extract – Rhodiola rosea extract – Humulus lupulus extract – Schisandra chinensis extract – Bacopa monnieri extract – Panax ginseng extract – Valeriana officinalis extract – green tea extract and L-theanine – Centella asiatica (gotu kola) extract	– Hypericum perforatum extract (St. John's wort) – Crocus sattivus (saffron) flower extract – Melissa officinalis extract – Crateugus (hawthorn) fruit extract – Lavandula sp. extract – Withania somnifera (ashwagandha) extract – Rhodiola rosea extract – Humulus lupulus extract – Schisandra chinensis extract – Valeriana officinalis extract – green tea extract and L-theanine – Centella asiatica (gotu kola) extract – Ocimum tenuiflorum (tulsi) extract – Passiflora incarnata extract – hemp (±THC) – Convolvulus arvensis extract – Matricaria chamomilla extract

For each of the mentioned herbal ingredients number of preparations containing a given ingredient was calculated to find 10 most popular ingredients for further consideration. At the same producer's/merchant's declarations as to expected effects were analysed. The results of these analyses are presented in Table 2.

Table 2. Occurrence of herbal ingredients in preparations intended to improve mood or reduce the effects of stress and effects declared by producers/merchants.

Herbal ingredient	No. of preparations with the ingredient		Effects declared by producers/merchants
	mood	stress	
Withania somnifera (ashwagandha) extract	22	16	– decrease in cortisol levels – reduction of the effects of stress – mood improvement – positive effect on sleep
Melissa officinalis extract	11	21	– reduction of anxiety and stress – positive mood maintenance – facilitating sleep
Rhodiola rosea extract	8	13	– resilience at the time of stress – mood improvement – cognitive functions improvement – positive effect on sleep
Humulus lupulus extract	6	13	– anxiolytic effect – facilitating sleep – sleep quality improvement
Valeriana officinalis extract	4	11	– anxiolytic effect – reduction of nervous tension – positive effect on sleep

Crocus sattivus (saffron) flower extract	11	1	– reduction of the effects of stress – positive mood restoration and maintenance – easing PMS symptoms
Lavandula sp. extract	3	3	– facilitation of relaxation – healthy sleep maintenance
Passiflora incarnata extract	0	6	– calming effect in states of emotional tension – facilitating relaxation – positive effect on sleep
Hypericum perforatum (St. John's wort) extract	4	1	– reduction of temporary states of nervous exhaustion/emotional tensions – short-term treatment of symptoms of mild depressive disorders
Schisandra chinensis extract	3	2	– resilience to stressors

3. CURRENT STATE OF KNOWLEDGE

Withania somnifera (ashwagandha)

W. somnifera (ashwagandha) is said to have several positive effects on stress, mood and sleep. Based on double-blind randomized clinical studies [23-25] it is supposed to decrease the level of cortisol as a biomarker of stress. It also decreased perceived stress, anxiety and depression measured with Perceived Stress Scale (PSS), Hamilton-Anxiety Scale (HAM-A) and Depression, Anxiety and Stress Scale-21 (DASS-21) [24,25]. In a prospective study Chandrasekhar et al. [23] drew the conclusion that 60-day intake of 300 mg of W. somnifera may increase resistance to everyday stress in chronically stressed individuals basing on decreased cortisol level and improved results in PSS, DASS and General Health Questionnaire-28 (GHQ-28). The exact mechanism of anti-stress and anti-anxiety action of W. somnifera is unknown, but the hypotheses include the modulation of hypothalamic-pituitary-adrenal axis, enhancement of acetylcholinesterase activity in lateral septum and globus pallidus, modulation of muscarinic receptors and reversed glutamate-evoked stress by upregulation of Hsp70 [26,27]. In terms of sleep quality improvement, the effect was obtained in few studies performed on animal models [28] or in small human trials [29,30]. The results seem promising, but insufficient to confirm effectiveness and safety of W. somnifera in this indication [30]. Finally, the postulated antidepressant effect needs further investigation [24]. It must be noted that that W. somnifera contains more than 140 compounds and involves different extraction methods leading to a considerable heterogeneity and making it difficult to objectively assess its effectiveness in the given indications [27].

Melissa officinalis

Among different herbal ingredients, M. officinalis is one of the most well-researched. It is advertised as an anxiolytic and sedative agent, as well as a sleep-aid and mood-enhancer. Its effect on anxiety and depressed mood is quite well-established [31]. Decreased stress levels were obtained in double-blind randomized trials on healthy individuals [32], patients with chronic somatic diseases [33,34], patients with trauma injuries [35] and finally among patients diagnosed with mild or moderate anxiety disorders and sleep disturbances [36]. As for the mechanism of action, it is proposed that M. officinalis inhibits GABA breakdown and stimulates cholinergic and GABA-A receptors [37]. Its antidepressant effect was obtained in a series of human trials [38,39,40], one of which compared M. officinalis with fluoxetine. In this double-blind randomized study similar therapeutic results were achieved in patients with mild to moderate depression taking M. officinalis and fluoxetine [40].

Rhodiola rosea

In the recent years R. rosea has become a very popular substance with postulated antidepressant, anxiolytic, sleep-promoting and procognitive effects. Most of the analysed preparations mentioned R. rosea as a stress-relieving substance and it seems to be justified in terms of evidence-based knowledge [41]. In human trials it was proven to ease distress and stress-related symptoms such as tiredness and exhaustion [42], also in individuals with burn-out syndrome [43]. In a study by Edwards et al. [44] a preparation of R. rosea was distributed over the period of 28 days to 101 outpatients with high levels of stress, leading to significant improvement in stress symptoms, fatigue, mood, concentration and quality of life (measured by appropriate questionnaires). The exact mechanism of action is, like with most herbal ingredients, not fully known, however impact on ATP production in mitochondria, ion channel modulation and hormone release normalisation are suggested [45,46]. In a series of clinical trials R. rosea was also noted to improve attention, speed and accuracy of task performance in stressful circumstances [47]. The effect was observed even after intake of a single dosage [48]. Along with cognitive functions improvement it also seems to have a positive effect on physical fitness [49,50]. When it comes to mood improvement, the evidence is limited to single trials conducted in individuals already diagnosed with a depressive disorder [51,52,53]. The literature on sleep-facilitating effect of R. rosea is also scarce and conflicting [54,55]

Humulus lupulus (hops)

H. lupulus is broadly advertised as a sleep-facilitating substance. However, it is problematic to verify this declaration due to the fact that in many trials H. lupulus was administered along with Valeriana officinalis [56,57]. In a single study such a combination was proven to be as effective as benzodiazepines in patients with sleep disorders [58]. However, later work of Cornu et al. [59] argued H. lupulus does not differ from placebo in patients with insomnia. Also, studies varied in objectives and course. In terms of anxiolytic, sedative and mood-improving action, H. lupulus is believed to interact with specific subtypes of 5-HT receptors and melatonin receptors, as well as to influence GABA-ergic neurotransmission [60,61]. In a randomized, double-blind trial in young individuals reporting mild depressive, anxiety or stress symptoms a significant decrease in depressive and anxiety (measured in DASS) was observed after 4-week administration of the preparation containing H. lupulus extract [62], however its effectiveness and safety needs more investigation [63].

Valeriana officinalis

V. officinalis can mostly be found in preparations intended to reduce negative effects of stress. In a series of studies it was proven to decrease reactivity to stressful situations in adults, in most cases measured by State-Trait Anxiety Inventory (STAI) and/or HAM-A [64,65]. GABA, adenosine and dopamine transmission are believed to be involved in the process. However, the substance's effectiveness in individuals with the diagnosis of anxiety disorders was not supported by scientific evidence [64,66]. There are very conflicting reports as to whether V. officinalis improves the quality of sleep [67,68,69,70,71].

Crocus sattivus (saffron)

On the Polish market for dietary supplements, C. sattivus is mainly included in preparations intended to improve mood. This effect was investigated in a number of human trials, whose results support the idea that saffron extract may decrease depressive symptoms [72-74]. However, it should not be used as the sole treatment for depressive disorders [75]. In terms of the postulated anti-stress effect, it is suggested that C. sattivus decreases corticotropine (CRH) expression and thus exerts a protective effect on cognitive functions, exhibits oxidative stress and decreases stress-induced corticosterone plasma level. It must be clearly emphasized that these effects were obtained in mice and in molecular laboratory settings (C. sattivus protein extraction), rather than in human models [76,77]. Saf-

fron's positive effect on premenstrual syndrome (PMS) symptoms was also considered with several double-blind randomised trials giving confirmatory results [73,78,79].

Lavandula sp.

Lavandula is available in the form of oral preparations or oils for inhalations, with the former being recommended in long-term treatment and the latter being superior in short term [80]. For the aim of this review only oral preparations were taken into consideration, since aromatic oils are not sold as dietary supplements in Poland. The anxiolytic and sedative effect of Lavandula extract is well proven [81]. Studies confirming its effectiveness in anxiety reduction were performed both in individuals with "subsyndromal" anxiety disorder (i.e. anxiety disorder NOS according to DSM-IV) [82] and individuals with diagnosed anxiety disorders [83,84,85]. Interestingly, in a multi-centre, randomized trial Lavandula extract was proven to be comparably effective in reducing anxiety levels in patients with generalized anxiety disorder as lorazepam, with Lavandula extract having no significant adverse effects and no sedation effect [86]. As for the mechanism, Lavandula is mainly thought to affect serotoninergic system [87,88]. In terms of its effect on sleep, a few important aspects must be noted. First, it is noticeable that most of the trials were conducted on small groups and/or were retrospective in nature [89,90,91]. Also, they varied in terms of the used formulations, with Lavandula aromatherapy being the most popular.

Passiflora incarnata

On the Polish market P. incarnata can be found in preparations intended to reduce the effects of stress. Human trials suggest that P. incarnata is effective in reducing anxiety [92]. It is also described as effective premedication before spinal anaesthesia and surgeries [93,94]. In a study by Azimaraghi et al. [95] patients who were administered P. incarnata experienced lower pre-operative anxiety than those who were given oxazepam. Interestingly, P. incarnata was also proven to be an effective add-on treatment during benzodiazepine tapering [96]. One of the postulated mechanisms of action of P. incarnata is through modulation of GABA-A receptors (partial agonism) [97].

Hypericum perforatum (St. John's wort)

The psychopharmacology of H. perforatum has been extensively studied in human trials. It is mostly sold as a self-care preparation for depressed mood. Evidence suggesting its antidepressant action can be found in the literature [98,99]. A meta-analysis of trials conducted on patients with mild or moderate major depressive disorder showed that H. perforatum is more effective than placebo and comparably effective as tricyclic antidepressants, tetracyclic antidepressants and selective serotonin reuptake inhibitors (SSRI), at the same time having less adverse reactions [100]. The postulated mechanism of action is, among others, inhibition of serotonin, dopamine and noradrenaline reuptake, MAO inhibition, β-adrenergic modulation and inhibition of glutamate release [101,102]. The postulated reduction of stress (along with consequent diminished cognitive impairment) was described predominantly in animal models [103,104,105] or in case reports [106]. Kobak et al. [107] found H. perforatum effective in social phobia. Much attention is paid to safety issues, as H. perforatum has a huge potential to interact with many medications [108].

Schisandra chinensis

S. chinensis extract is advertised as a stress reliever. However, its effects were mainly demonstrated in animal models [109,110,111]. The proposed mechanism of action is HPA axis modulation as well as serotoninergic, dopaminergic, noradrenergic and GABA-ergic systems modulation [112].

4. DISCUSSION

Several conclusions can be drawn from the analysis of the Polish market for dietary supplements intended to improve mood or reduce

the effects of stress. First of all, it is noticeable that choice of such preparations is very huge, with the selected 100 products (50 per each indication) being only a small representation of the whole market. The underlying causes of using psychotropic dietary supplements need to be investigated in details, but presumably they involve deterioration in mental wellbeing in Poland (e.g. due to COVID-19, recession and war in Ukraine) [113,114,115], high preoccupation with one's mental health (39%) [116], low accessibility of mental health services (defined as the number of psychiatrists per inhabitants, psychiatric hospital beds, share of people consulting psychologists) in comparison to other EU countries [117] and social stigma of mental illness [118]. It is worth noting that according to the Supreme Audit Office, the market for dietary supplements is a high-risk area with insufficient control [119]. This, combined with the fact that many dietary supplements are addressing psychopathological problems, creates the need to address this phenomenon from the scientific point of view in further studies.

Although herbal ingredients are generally thought to have a more moderate effect and less adverse reactions, in certain circumstances they may pose a threat to an individual's health, especially when taken along with prescription medications or by individuals with comorbidities. Examples include W. somnifera in autoimmune and thyroid diseases [120] and H. perforatum in thyroid diseases [121]. As for H. perforatum, it may also cause hypersensitivity to sunlight, leading to sunburns or fotoallergic reactions during the therapy and 14 days after its completion. If taken along with antidepressant drugs, it may lead to serotonin syndrome [122].

Unfortunately, the exact pharmacokinetics and pharmacodynamics of herbal ingredients remain unknown in many cases, which makes it impossible to identify and test particular interactions. Hypothetically, they may interact with any substances that are metabolised by the same CYP450 [123], which in many cases (e.g. H. perforatum) leads to a long list of potential interactions [124]. Due to similarity of expected effects, herbal ingredients are generally not recommended to be used in parallel with antidepressant, anxiolytic, sedative and hypnotic medications, especially without doctor's knowledge [125]. Also, it is impossible to draw conclusions as to optimal dosages and time of therapy, as the preparations used in the trials vary considerably in terms of active constituents' content (e.g. withanolides for W. somnifera), chemical composition or duration of intake. No official guidelines specifying the dosage of herbal substances and the suggested duration of treatment are currently available.

The problem is probably compounded by lack of education in the field of food and drug safety. Given the general low level of knowledge about dietary supplements among Polish adults [126], it emerges as a serious problem, especially in the specific context of mental health and when faced with little control over the quality of dietary supplements in Poland.

The market analysis also revealed very imprecise, subjective and unverifiable declarations of producents or merchants of the preparations, such as "supports the maintenance of mental health", "helps soothe your nerves", "revitalizes nerves and brain cells", "helps in relaxation", "stabilizes behavioural patterns", "maintains normal mind functions", which may make it difficult or even impossible for an individual to assess the preparation's effectiveness and potentially delay optimal treatment. An attempt to verify these declarations with medical literature shows that often they come out unjustified.

Thorough research should be conducted in order to estimate the popularity of preparations intended to improve mood or reduce the effects of stress among Polish adults, to build a demographic characteristic of this group and to identify potentially hazardous behaviour patterns (e.g. intake of several preparations at the same time, not informing GPs/specialists about the use of preparations). If needed, educational measures should be taken to increase the level of knowledge and encourage people to make informed decisions based on evidence-based knowledge, while also providing them with popularised sources of information they could easily comprehend.

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