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Natural products of relevance in the prevention and supportive treatment of depression

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Summary

The use of herbs or their parts: leaves, roots, rhizomes, flowers, seeds, natural strains, as well as extracts or isolated metabolites is becoming more and more popular. Natural remedies not only act prophylactically, but also help to alleviate symptoms of many diseases and enhance the overall functioning of the internal organs. Many raw materials of natural origin plays a role in treatment of health problems, and also in case of serious diseases such as depression. Depression (affective disorder) now affects about 10% of the population, but in next few years due to the development of civilization and increasing pace of life, the probable number of people suffering from this disease can grow rapidly. Natural raw materials such as Bacopa monnieri, Crocus sativus, Eleutherococcus senticosus, Griffonia simplicifolia, Hypericum perforatum, Sceletium tortuosum, Piper methysticum, Rhodiola rosea, Aspalathus linearis, Camellia sinensis, Ficus carica, Lycium chinense, Cuminum cyminum, Panax Ginseng can effectively assist the prevention and treatment of depression. Daily diet may also have positive effect in prevention of this disease. It was found that 5-hydroxy-L-tryptophan, L-tryptophan (which are precursors of serotonin in the CNS), omega-3 fatty acids and anthranilic acid (vitamin L1) are able to improve mood. L-Tryptophan, 5-hydroxy-L-tryptophan are present in the largest quantities in the fruiting bodies of edible mushrooms. Omega-3 fatty acids are found in the flesh of fish, walnuts, soybeans, beans and chicken egg protein, while the anthranilic acid is commonly found in plants.

Key words: plants and mushrooms in prevention of depression, 5-hydroxy-L-tryptophan, anthranilic acid

The study was not sponsored

Introduction

Healing with herbs has a story as long as the human history itself, Neanderthal tombs show the presence of aromatic herbs – ones that are currently documented as medicinal herbs. Using herbs or their parts: leaves, roots, rhizomes, flowers, seeds, thallus, as well as their extracts or natural material isolated metabolites can act both as a prophylaxis or a cure to diseases and enhance general organs functioning especially immunologic system. Many herbs have a role in curing mood disorders. Depression (affective disease) has many types [1]. Contracting depression is becomes a world problem. Data gathered by World Health Organisation (WHO) and World Bank clearly show it. It can be seen that depression is the fourth most dangerous disease (currently it is estimated that 10% of population is afflicted) leading to death or disablement, it is also estimated that up to year 2020 depression will be the second most dangerous disease – less dangerous only than cardiac ischemia [2]. It is an important social problem, because patients have a decreased work activity or cannot work at all [3–5]. Natural cures (drugs) have different active compounds that may help to treat the condition holistically acting on the body of the patient, the more that depression affects the whole body, causing multi-organ dysfunction. The need for effective and well tolerated remedies for depression has influenced scientists to more strict analysis of herb drugs and natural products which are traditionally used for depression treatment.

Aim

The goal of this paper is to show natural products that are effective in depression and mood disorders prophylaxis. Currently, one of the most effective plants used as antidepressants are: Bacopa monnieri (Water hysop) – Brahmi, Crocus sativus (Saffron), Eleutherococcus senticosus (Siberian Ginseng), Griffonia simplicifolia (Griffonia), Hypericum perforatum (St John's wort), Sceletium tortuosum (Channa), Piper methysticum (kava kava), Rhodiola rosea (Golden Root). Less important are: Aspalathus linearis (Rooibos), Camellia sinensis (Tea leaf), Ficus carica (Fig leaf), Lycium chinense (Wolfberry), Cuminum cyminum (Cumin Seed), Panax Ginseng (Ginseng), Schisandra chinensis. Additionally plants that have a sedative effect are also used: Valeriana officinalis (Valerian), Passiflora incarnata (maypop, purple passionflower), Lavandula angustifolia (lavender), Melissa officinalis (lemon balm), Leonurus cardiaca (motherwort), and Humulus lupulus (common hop). Considering large indole compounds, especially L-tryptophan and 5-hydroxytryptophan (5-HTP), mushrooms fruiting bodies can also have a meaning in prophylaxis. Current research shows, that diet is also important in depression prevention e.g. it is advisable to avoid alcohol, sugar excess, foods abundant in starch, because all this factors increase blood glucose level [6]. After a short time glucose level suddenly begins to drop what causes

fear anxiety and depression [7]. "Feeding Minds" rapport showed that in recent years British Islands noted a one-third decrease in fruits and vegetables consumption, what caused an increased susceptibility to depression. It was found that 5-hydroxy-L-tryptophan, L-tryptophan as a serotonin precursor in CNS, anthranilic acid (vitamin L_1) and fatty acids decrease the risk of depression development. Researchers report that there is a connection between omega-3 acids level in human diet and depression prevalence [8–11]. L-tryptophan is an relatively exogenous amino acid, that takes part in building proteins in living organism. Exogenous amino acids have to be supplied in diet. L-tryptophan takes part in synthesis of vitamin B_3, melatonin and serotonin. This amino acid and its derivative play an important role in pain perception and regulation of mood and sleep [12, 13]. L-tryptophan is a precursor of 5-hydroksy-L-tryptophan (5-HTP) which is a direct substrate for serotonin synthesis. Ingestion of this amino acid increases brain produced 5-HTP level. The best source of L-tryptophan and 5-hydroxy-L-tryptophan are mushrooms fruiting bodies [14–18]. Anthranilic acid as a precursor of L-tryptophan commonly occur in plant foods and shows a synergism with vitamin B_6, C, antidepressants and sedative substances. Omega-3 fatty acids can be found in fish meat, linen oil, peanut oil, canola oil, almonds, walnuts, seafood, soya and beans. Vitamins from B group are also important – showing beneficial action to the nervous system, occurring mainly in buckwheat, green vegetables, wholemeal bread and nuts.

Plant materials with an antidepressant effect

Bacopa monnieri

Bacopa monnieri (L.) Pennell (Water hyssop), commonly known in India as Brahmi or Jalanimba is one of the most important plants in traditional Hindi medicine – Ajurveda. The name of the plant itself comes from word Brahma one of the main Indian deities. It is used since 5,000 years in epilepsies, insomnia and as a sedative and relaxant. Indian Materia Medica (Bhavprakasha Nighantu year 1 500) points this plant to be a remedy for memory and concentration loss [19, 20]. Commercial drugs containing B. monnieri aid brain function, improving concentration and memory both in young and elderly people [21]. Clinical researches confirm beneficial effects of this herb in children suffering from ADHD and improving the cognitive functions after brain strokes and epilepsies. Current researches indicate that effects of these plant extracts are caused by the ability to modulate cholinergic system [22]. Effects of B. monnieri is thought to be caused by bacosides, triterpenoids with steroid saponin groups [21]. Bacoside A consists of 3 saponins: bacogenin A1, A2 and A3 (A3 predominates) (Figure 1) [23].

This plant is used as an adjuvant in neurodegenerative disorders such as Alzheimer or Parkinson diseases. On the basis of the research on the depression patients, it was

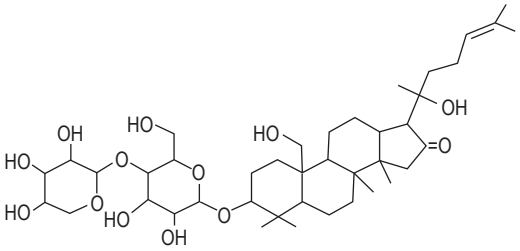

Figure 1. **Bacoside A3**

shown that B. monnieri extracts (in a 300 mg dose) show an antidepressant effect [21]. Although it is not clear if the process is caused by serotoninergic or GABAergic neurotransmission [24]. It is suggested that the effect comes from bacosides induced increase of dopamine and serotonin level [22]. In rats the antidepressant effect (in Porsolt forced swim test and "learned helplessness tests") can be compared with a synthetic drug – imipramine [24]. It is shown that B. monnieri substances showing antidepressant effect contain pseudo-jujubogenin (i.e. bacopasides I, II and bacosaponin C) as a specific aglycone group, on the other hand compounds containing jujubogenin (bacopasid VII) did not procure antidepressant effect [25]. Some other researches did not show statistically significant differences between B. monnieri and placebo in decreasing depression level [22]. Probable mechanism of B. monnieri extracts effect on cholinergic system comes from AChE (acetylcholinesterase) inhibition in brain cortex (especially in parietal lobe and hippocampus). This action causes increased acetylcholine availability in mentioned areas and leads to an increase of cognitive abilities [26]. Furthermore, it was shown that 8-weeks long administration of B. monnieri produces a 25% increase in brain blood flow in rats, with the systolic blood pressure remaining on a constant level. This plant also induces vasodilatation in basilar and mesenteric artery, but poorly influences femoral and kidney arteries. Lack of hypertensive or hypotensive effect determines that B. monnieri can be applied as a food supplement with nootropic effect [27]. B. monnieri extract decreases morphine and phenytoin toxicity. Large doses of this plant increase T4 hormone concentration in mice. T3 level is not influenced what suggests direct influence on T4 synthesis or release by B. monnieri extract. It should also be noted that large doses of extract (200 mg/kg) were used, what suggests that typical supplementation (200–400 mg) in humans may not produce T4 concentration increase. Products containing Bacopa monnieri are: Pamicon, Brahmi (extract from the leaves of B. monnieri), LogiQ (extract from the leaves of B. monnieri and leaf extract of Centella asiatica in capsules), Super IQ (powdered leaves of B. monnieri in capsules). B. monnieri extracts standardized for content of saponins (bacosides). B. monnieri does not provoke any adverse effects [28].

Crocus sativus

Crocus sativus L. (Saffron) – monocotyledonous plant from Iridaceae family. Chinese name of saffron is Fan-Hong-Hua. Although its wild form is unknown, most probably it origins from south-eastern Europe or Minor Asia. Saffron have been grown for centuries and its dried pistils are the most expensive and noble spice in the world. The plant is also used as a dye by Buddhist monks for clothes dyeing. Saffron occurs in two forms: ground and whole pistils [29]. Antispasmodic, digestive, appetite increasing and mood improving effects are the longest known effects of saffron. Saffron is a medicinal herb thought to be a panacea in countries of origin. Apart from antidepressant effects saffron has also been found to have anti-cancer, expectorant, anticonvulsive, antibacterial and antioxidative effects. In cosmetics saffron is used in rejuvenation formulations, because of its antioxidative effect. The herb is also used as an aphrodisiac [30]. Collecting 1 kg of pistils takes 150,000 flowers and 40 hours of work [29]. Obtaining saffron is highly work consuming because everything is being done manually. This plant is mainly cultivated in Mediterranean Sea area and Iran up to India. Antidepressant effect comes from an increase of serotonin and dopamine level in CNS, what causes mood increase. Saffron contains above 150 aromatic volatile compounds. Main active substances are crocetin (Figure 2) and its derivates, zeaxanthin, lycopene, α – and β-carotene – orange dyes from carotenoids family.

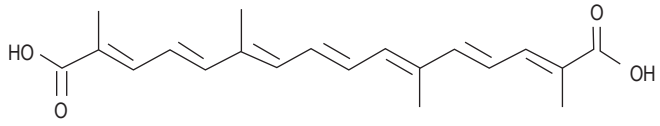

Figure 2. **Crocetin**

Other active compounds are flavonoids and safranal (Figure 3), a volatile compound, which is responsible for the herbs' characteristic flavour. Safranal is produced during drying from bitter glycoside picrocrocin degradation [30, 31]. The effect of saffron is comparable to synthetic antidepressants: fluoxetine and imipramine [32–34].

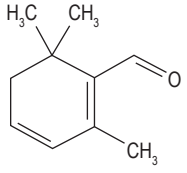

Figure 3. **Safranal**

Saffron, apart from antidepressant effect, also relives PMS (pre-menstrual syndrome) symptoms. Research showed that 75% of 25–45 years old women afflicted by PMS declared a better mood after receiving saffron extract. In double blind randomized trials it was shown that 30 mg of saffron extract (in capsules) administered for 6 weeks gives a considerable decrease in depressive symptoms compared to placebo. The research was conducted on adults with diagnosed depression (17 in 23 points Hamilton scale). Patients were divided into two groups one was administered with 30 mg of Crocus sativus extract, the other with placebo. After 6 weeks the result on Hamilton scale was 10 in patients taking saffron and 19 in the group taking placebo. In this research no significant differences in adverse effects between both treatments were observed [35]. Second almost identical research was conducted with comparison to fluoxetine (antidepressant) 20 mg/day. The results did not show significant differences between saffron and synthetic drug, both in depression treatment and adverse effects [33]. On the basis of this research it was proven that crocin and safranal inhibit reuptake of dopamine, noradrenalin and serotonin. Safranal is an efficient anticonvulsant .It was shown that it acts as a GABAA receptor agonist [33, 35]. It is also an antioxidant and shows in vitro cytotoxicity to cancer cells [36]. Other plant sources of safranal which also show antidepressant effect are Aspalathus linearis (Rooibos), Camellia sinensis (Tea leaf), Ficus carica (Fig leaf), Lycium chinense (Wolfberry), Cuminum cyminum (Cumin Seed) [36]. Available homeopathic formulation in Poland with this material is Boiron Crocus sativus; another formulation is Forsen containing 30 mg of extract of Crocus sativus. Saffron taken in high doses may increase the risk of miscarriage, and therefore it cannot be used by pregnant women without consulting a doctor. It is not recommended for children. Saffron overdose is dangerous, it causes vomiting, diarrhoea, bleeding from the gastrointestinal tract and urogenital system.

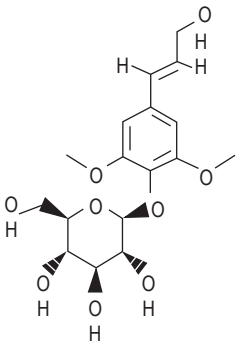

Figure 4. **Eleutheroside B**

Eleutherococcus senticosus

Eleutherococcus senticosus (Ruprecht & Maximowicz) Carl Maximowicz (Acanthopanax senticosus Harms), Araliaceae family, commonly known as Siberian Ginseng or Eleuthero Ginseng is a dicotyledonous with adaptogenic properties. This plant occurs in north-eastern Asia (China, Japan, Asiatic part of Russia and Mongolia). The best commercial farms can be found in Russia and China. Main physiologically active compounds are eleutherosides (phenolic glycosides), lignans, saponin glycosides, oleanolic acid derivatives – senticosides A–F, steroid saponins – eleutheroside A, syringin – eleutheroside B (Figure 4), eleutheroside B1 which is an isofraxidine glycoside (isofraxidine-7-O-alfa-L-glucoside), also commonly known as beta-calicanthoside, eleutheroside B2 which is coumarin, eleutheroside B4 – sesamin, syringaresinol – eleutheroside D also known as acanthoside D, a lignan, eleutherosides E, I, K, L, M (eleutherosides I–M are triterpene saponins: eleutheroside I – common name musenin B, eleutheroside M – hederasaponin) [37, 38].

Siberian ginseng roots contain from 0.6 to 0.9% of eleutherosides and stems from 0.6 to 1.5%. Furthermore, the plant also contains: caffeic acid, caffeic acid ethyl ester, coniferyl aldehyde, sinapyl alcohol, beta-sitosterol, beta-carotene, vitamin E (tocopherol), carbohydrates (galactose, arabinose, β-maltose, α – and β-glucose, sucrose, and polysaccharides – eleutheranes). Elutherococcus extracts, rich in fitosterol, have an adaptogenic, antidepressant and anxiolytic effect, aid learning processes, memorizing and also show detoxicant, anti-inflammatory, antioxidative, hypoglycaemic and diuretic effect. Plant extracts are standardized for eleutherosides A–G and I–M content. Antidepressant effect was examined on rats subjected to neuropharmacological tests. The tests were prepared on the basis of antagonistic activity to reserpine, clofeline and L-DOPA. Eleutherococcus senticosus extract caused a 56.4% decrease in activity during rats immobilization, which was slightly smaller than in case of amitriptyline (73.5%) [39]. It also removes stress caused by treatment with steroids (cortisone). Lifeplan is currently a drug containing Elutherococcus extract (600 mg); Immunostin – liquid extract from the roots of Eleutherococcus and Stress Control containing 33.3 mg of Eleuterococcus extract, preparations standardized for the content of eleutherosides. At the recommended doses, Eleutherococcus does not give any side effects. Interaction with other plants and supplements: unknown.

Griffonia simplicifolia

Griffonia simplicifolia (Bandeiraea simplicifolia Benth.) from Fabaceae family from dicotyledonous class is a bush common in west and central Africa (Ghana, Ivory Coast, Togo). In forests it can take form of a climbing plant, especially when growing near to tall trees. Griffonia can grow up to 3 meters. Flowers produce black fruits with seeds that can be used as a source of 5-hydroxytryptophan (5-HTP). Seeds contain

about 6–14% of 5-HTP, additionally plant leaves contain serotonin in concentrations 0.1–0.2%. Other active compound is griffonin (a cyanoglucoside of lithospermoside) isolated from roots used in sickle-cell anaemia treatment. Griffonia simplicifolia roots also contain many lectins e.g. B4 lectin is used for marking sensor neurons in neurologic research [40]. The herb is procured only from natural state, because up to this moment there are no commercial plantations. Traditionally in Africa, stems and roots in form of small sticks are chewed and leaves are applied on wounds which are hard to heal. The plant juice is used in urinary tract diseases. Decocts from stems and leaves are applied as antiemetic drugs. G. simplicifolia is also used as an antibiotic and aphrodisiac. The research showed, that the plant extracts increase serotonin brain level. In some countries (United Kingdom, USA, Canada, and Germany) after an industrial extraction a 95–98% 5-HTP extract is obtained, mixed with vitamins and packed into capsules or mixed with green tea or yerba mate. In this form Griffonia extracts are used as dietary supplements aiding depression treatment, appetite reduction and sleep induction. This products most commonly contain 50–100 mg of 5-HTP [13, 41]. Ingested 5-HTP easily crosses BBB and is converted to serotonin in CNS. During the absorption of 5-HTP there is no need for special transport molecule. The absorption is also not influenced by amino acids, what allows 5-HTP to be administered with meals, without losing its efficacy. This compound is well absorbed after oral administration (70% of the dose is introduced to bloodstream). It was proven, that therapeutic administration of 5-HTP may be efficient in depression, fibromyalgia, chronic head pains and insomnia [12, 42]. Available products containing G. simplicifolia: Maxivit Diet (extract from seeds – 20 mg); Griffonia Seed Extract, standardized for 5-HTP content. When applying G. simplicifolia should not be taken with antidepressants from the selective serotonin reuptake inhibitors group.

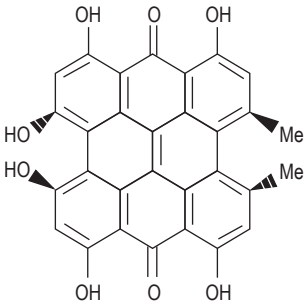

Figure 5. **Hypericin**

Hypericum perforatum

Hypericum perforatum L. (St John's wort) (Hypericaceae family – dicotyledonous) naturally occurs in Europe, western Asia and north Africa. It was introduced to North America, South America, southern Africa, Australia, New Zealand and Japan. In superficial parts, apart from numerous active compounds such as flavonoids (mono – and dimeric), xanthones, phenolic acids, hypericin (Figure 5), hyperforin, terpenes (aromatic oils),the plant contains indole compounds, such as melatonin. All this metabolites groups are a frequent object of phytochemical, pharmacological and biotechnological research. The antidepressant effect was initially connected to hypericin and later to hyperforin. Hypericin action was supposed to come from MAO inhibition. Later MAO inhibition was also observed in in vitro studies for biflavonoides [43].

Newer researches showed that hyperforin inhibits reuptake of serotonin, adrenaline, noradrenaline, GABA and L-glutamate [44]. Considering this differences Hypericum extracts are most commonly used and they are considered to be the best form of this herb. Antidepressant effect can be observed for ethanolic and oleic extracts (both contain hypericin (naphthodianthrone), hyperforin (triphenole derivative), bioflavonoids and xanthones). Plant extracts inhibit serotonin reuptake in synaptic gaps and also act as MAO inhibitors [45]. Other mechanism of hypericin action is increasing the light sensitivity of human organism. High concentration of melatonin in H. perforatum allows for the use of this herb in neurologic diseases. The melatonin role in higher plants physiology is not entirely discovered. There is a theory that both serotonin and melatonin, similarly as in mammals, are a circadian rhythm and year cycle regulator, as well as an antioxidant [46]. Research conducted on in vitro cultures of this species were supposed to analyse melatonin and serotonin biosynthesis from tryptophan as a precursor [46, 47]. Hypericum herb is a source of kynurenic acid, which is responsible for adaptation processes in human organism. Kynurenic acid is present in all mammals organs, the biggest concentration can be found in liver cells and smaller amounts can be found in brain tissue. Kynurenic acid causes dose dependant hypotonia and acts as a neuroprotective agent in brain hypoxia. This substance is also an antidepressant. Meta-analysis of clinical researches conducted in 1996 showed that H. perforatum is considerably more effective than placebo and has an action comparable to available antidepressant drugs. Research was conducted on low or moderate depression (Linde 1996). In clinical research, influence of high doses (900 mg/day) of H. perforatum extract were compared to placebo and sertraline (an antidepressant, dose 50 mg/day). Depression was evaluated with Hamilton test (before treatment score was at least 20) and after 8 weeks of therapy. H. perforatum and sertraline showed similar results to placebo. Two aspects should be taken into consideration: administered H. perforatum form was not standardized on hyperforin, which is thought to be an important substance for depression treatment and the depression was too severe (Hamilton > 20) [48]. Products containing extracts from this material are usually standardized to hypericin

e.g.: Deprim Forte – 1 capsule contains 425 mg of standardized extract of St. John's wort which contain an average of 1 mg of total hypericin (0.75–1.3 mg), Nervomix Forte; Hyperherba; Depribon; Happy Plus; Silenil; Positivum; Hyperosedat; Perhip. St. John's wort may reduce the effectiveness of certain drugs. Due to the induction of cytochrome P-450, and the effect on the biotransformation of xenobiotics, hypericin may cause a reduction in the plasma concentration of some therapeutic drugs. This applies indynavir used in the treatment of HIV, warfarin, cyclosporine, oral contraceptives, dextromethorphan, theophylline, amitriptyline, digoxin and phenytoin. The active compounds occurring in the herb are potent inducers of CYP 3A4 in the gut wall and liver, which results in a significant increase in metabolism of simvastatin. A potential reduction in the concentration of midazolam in the body may also be linked with the induction of CYP 3A4. One of the most well-known side effects of St. John's wort are its photosensitizing properties [49].

Sceletium tortuosum

Sceletium tortuosum (L.) NE Brown – Kanna (Channa, Kougoed). A perennial plant from Aizoaceae family (earlier Mesembrynantheacae), dicotyledonous class. The plant comes from Kalahari Desert in RSA and is a succulent growing sideways close to the ground, up to one foot high. Other types of Sceletium (emarcidum, expansum, strictum) and Mesembryanthemum crystallinum are also interesting. Sceletium tortuosum has a long story of medicinal usage. In RSA from thousands of years it aids the hunting-gathering tribes of south Africa during several weeks long migrations in extreme desert climate. Hottentots in South Africa used Sceletium tortuosum, known as Kanna, as a relaxant intoxicant. First mentions about this plant usage are noted in 4th century. In RSA it is registered as a spasmolytic and antidepressant drug [50]. In 2010 FDA (Food and Drug Agency) allowed the use of Kanna as slimming drug. During last twenty years the interest in Kanna significantly increased and products with Kanna are used as a mild antidepressants. Kanna improves the mood, reduces fear, stress and tension. There were also experiments with using this plant in addiction therapies (alcohol, opiates). Sceletium tortuosum contains alkaloids: mesembrine, mesembrenone (isolated in 1914) (Figure 6), as well as mesembranol, tortuosamine and sceletenone [50].

Among these alkaloids the biggest antidepressant activity can be observed for mesembrine. This substance is a selective inhibitor of serotonin reuptake and inhibits phosphodiesterase 4. Mesembrenone has a similar but weaker effect. Other species of Sceletium – S. strictum – contains demethylmesembrenol, demetylmesembranol, mesembrenol, mesembrine, mesembranol and mesembrenone. The research conducted in 1932 showed that Sceletium tortuosum contains 0.3 and 0.86% of mesembrine in leaves and stem respectively. Other research stated that the mesembrine concentration in this plant is 0.7% and mesembrenine 0.2% [51].

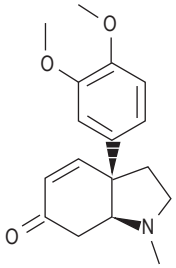

Figure 6. **Mesembrenone**

Piper methysticum

Piper methysticum (Kava kava, yaqona, sakau) – (Piper: Latin – pepper, methysticum: Greek – intoxicating) is a dicotyledonous plant from Piperaceae family. The plant has its origin in Micronesia and Vanuatu islands on Western Pacific. P. methysticum is an antidepressant plant. It was discovered that the constituents of Kava kava; kavain (Figure 7), dihydrokavain and dihydromethisticine are weak MAO inhibitors in vitro [52].

This plant cannot be used simultaneously with other MAO inhibitors such as ephedrine, Oenothera oil, Fenugreek, Ginkgo biloba, Lupulus, St John's wort, tyrosine, Valeriana, 5-HTP, DHEA (dehydroepiandrosterone), DLPA (phenylalanine DL), SAM (S-adenosylmethionine), vitamin B_6, chromium. Kava usage can provoke excessive sleepiness, when used together with drugs from serotonin group. P. methysticum influence on anxiety and depression was researched in a group of 60 adults for two weeks. Research plan stated that patients were divided into two groups. One group received one week therapy with drug and then placebo, second group placebo for one week and then the drug. In both cases 250 mg of kavalactones/day dose was used. The results (depression was measured using Montgomery-Åsberg Depression Rating Scale) showed that the placebo-drug method is considerably more efficient than the drug-placebo set. The researchers did not state weather the antidepressant effect of Kava is caused by the anxiolytic effect or it is a specific antidepressant one [53]. Under the Act of 20

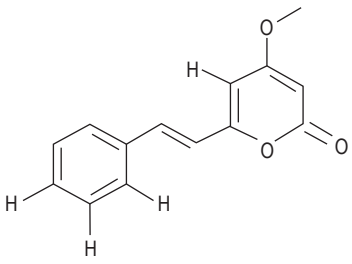

Figure 7. **Kavain**

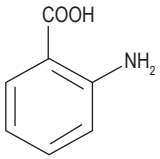

Figure 8. **Anthranilic acid**

March 2009 amending the Act on Counteracting Drug Addiction, possession of Kava kava living plants, dried fruit, seeds, extracts in Poland is illegal. Poland is the only EU country where the possession of this plant is completely prohibited.

Rhodiola rosea

Rhodiola rosea L. (Golden root) – Crassulaceae family, a dicotyledonous plant occurring in North America, Europe, Asia. In Poland it can be found only in Sudety and Karpaty mountains in the areas of national parks, it grows up to 40 cm and is able to endure high altitudes (2 280 m above mean sea level). The source of drugs from this adaptogenic plant is its rhizome with root. The plant contains numerous active compounds: salidroside glycosides, rosarin, rosavin, rosin, flavonoids, phenolic acid: gallic acid and chlorogenic acid (an antioxidant), organic acids (succinic, citric, malic, oxalic), taninns, anthraquinones [54]. Over few hundred years, R. rosea was used in Russia and Scandinavia as an energizing agent that increases physical and psychical endurance, preventing tiredness, depression, impotence and as a cure for tuberculosis [55]. In Swedish pharmacopoeia from 1755, there is a description of Rhodiola rosea application for depression due to its ability to enhance endurance and reliving tiredness. In latest research two doses of R. rosea extract were used (340 mg and 680 mg). Both doses in HAMD punctuation showed antidepressant activity against placebo. The research was conducted in a group of patients with mild and moderate deprssion (18–70 years old participants). It was found that Rhodiola extracts have a considerable antidepressant and hypnotic effect, as well as they can improve concentration, physical and mental endurance [56]. More extensive research upon this plant are needed to fully understand its antidepressant effect. Available products with this material are: Rhodiolin, CaliVita, Rhodiola, Naturell AB – a standardized extract of Rhodiola rosea root 200 mg (contains rosavins 6 mg). Although not shown to interact with other drugs in the case of R. rosea may occur addition of action with psycho-stimulants.

Many other plants are used as an aid in depression treatment. Due to hypnotic and tonic effect some raw materials, such as Valeriana officinalis radix, Passiflorae incarnata herba, Lavandule anqustifolia flos, Humuli lupulis trobillae, Leonuric ardiacae herba and Schisandrae chinensis fructus. Vitamin L_1 (anthranilic acid, 2-aminobenzoic acid – Figure 8) found commonly in plants described in 1930 by W. Nakahar is considered

by many authors as a factor necessary to lactation (L stands for Lactation). In plants it is used for L-tryptophan synthesis.

L-tryptophan can be immobilized in glycoside, can act as a reagent in aromatic amino acids reactions or it is used to indolo-3-acetic acid, protein and alkaloids biosynthesis. It is a precursor of tryptophan and serotonin, and therefore is used prophylactically to treat anxiety and depression at a dose of 0.5-1 g/day orally. Moreover, it shows synergy with vitamin B_6, vitamin C, antidepressant and sedative substances [12, 13].

Mushrooms as a source of tryptophan and its derivatives with an antidepressant effect

Considering an increase in mushrooms consumption both wild grown and cultivated, there is a necessity of analysis of secondary metabolites with a physiological importance for human organism. Edible mushrooms turned out to be an abundant source of indole type neurotransmitters precursors with an antidepressant effect such as L-tryptophan, 5-hydroxytryptophan, tryptamine, serotonin and melatonin.

It should also be pointed out that consumption of food containing edible mushrooms is safe and advantageous because they contain substances with health-promoting properties that protect human body against diseases of civilization. Analysis of some mushroom species show that even heat treated fruiting bodies of Cantharellus cibarius, Boletus badius, Lactarius deliciosus, Macrolepiota procera, Pleurotus ostreatus, and Suillus bovinus are an abundant source of bioactive indole compounds [17, 18]. The highest amount of serotonin from all analysed compounds was found in Cantharellus cibarius fruiting bodies (29.61 mg/100 g dry weight.). In Leccinum scabrum fruiting bodies the amount of serotonin was 13.09 mg/100 g dry weight. Species that also contain considerable amounts of these neurotransmitter are: Armillaria mellea, Boletus badius, Boletus edulis, Lactarius deliciosus and Pleurotus ostreatus. Although serotonin, when eaten, does not cross BBB, it can regulate intestines activity [41]. Serotonin, substance with multidirectional pharmacological activity, is a neurotransmitter in CNS and, together with melatonin, regulates circadian rhythm. Moreover it is produced not only in brain, but mainly in enterochromaffin cells. It is involved in smooth muscle contraction, regulates intestinal movements, influences blood pressure regulation, is involved in blood clotting and has an antioxidant effect [42]. Serotonin, generated endogenously in the brain, also plays an important role in regulation of sleep patterns, anxiety, aggression, body temperature, mood, course of pubescence process, cells regeneration and inhibition of cells aging, as well as it generally influences the immunological system of human organism. It also has a vasoconstrictive effect [12, 13]. Serotonin in asthmatic patients produces alveolar contraction. It is speculated that it also takes part in migraine pathogenesis and headaches connected to brain. Wide variety of serotonin dependent processes explains the existence of 7 types of serotonin receptors (5-HT) with several subtypes. Many classes of drugs

takes its action by serotonin receptors being agonist or antagonist or serotonin level modulators. Drugs acting through serotonin neurotransmission are antidepressants, anxiolytic antiemetic and migraine suppressors. According to recent research 5-HTP is a potential drug for Alzheimer's disease [41]. Information about indole occurrence in Basidiomycota species discusses mainly L-tryptophan which is biogenetic precursor of all indole compounds (e.g. dopamine, melatonin, serotonin, adrenalin) and vitamins (e.g. niacin) [42]. L-tryptophan content ranges from 0.16 g to 25.90 g/100 g dry weight (in fruiting bodies of S. bovinus before thermal processing) [14–18]. L-tryptophan is an exogenous compound for human organism that is why it must be ingested with food. Among extracts from mushrooms after thermal processing, Boletus fruiting bodies contained the highest amount of L-tryptophan – 17.71 mg/100 g dry weight. Edible mushrooms after thermal processing (especially S. bovinus) can be a L-tryptophan source and be an alternative to food obtained from animals. In case of B. edulis, L-tryptophan concentration was higher in processed material than in dried or fresh fruiting bodies. The reason behind this phenomenon can be that the indole compound such as serotonin, 5-hydroxytryptophan can decompose and form L-tryptophan, what is indicated by their high level in unprocessed B. edulis. Armillaria mellea fruiting bodies qualitatively analysed using HPLC method and then quantitatively marked by chromatographic-densitometry method showed serotonin, tryptamine and L-tryptophan content between 2.21 and 4.47 mg/100 g dry weight. Among marked indole compounds in fruiting bodies of Armillaria mellea, the biggest content was noted for L-tryptophan (4.47 mg/100 g dry weight) [15]. 5-hydroksytryptophan, a direct precursor of serotonin and melatonin was present in fruiting bodies both before and after thermal processing. However, the largest amounts were found in species of mushrooms before thermal processing. The maximum contents of this metabolite were found in extracts of unprocessed fruiting bodies of: L. edodes (24.83 mg/100 g dry weight), M. procera (22.94), S. bovinus (15.83) and in extracts of fruiting bodies of M. procera after thermal processing (10.11 mg/100 g dry weight). 5-methyltryptophan was found among unprocessed species only in L. scabrum, but in the highest content (8.32 mg/100 g dry weight). This compound has been demonstrated in processed fruiting bodies of four species: B. edulis, C. cibarius, L. deliciosus and P.ostreatus, in concentrations comparable to those found in the L. scabrum [14–18]. Melatonin was less frequently marked in examined mushrooms. It was found in small amount in extracts from fruiting bodies of B. edulis, C. cibarius, L. deliciosus, L. edodesi, M. procera (from 0.07 to 1.29 mg/100 g dry weight). In case of C. cibarius the amount of this substance after processing was the highest (4.40 mg/100 dry weight) [14–18].

It is proven that potential zinc role in depression treatment comes from modulating glutamate NMDA receptors, necessary for correct functioning of antidepressants. Lack of magnesium leads to important imbalances such as increased neuro-muscular activity. Natural sources of this elements are: cocoa seeds (Theobroma cacao) – cocoa,

bitter chocolate, nuts, dried fruits (apricots, figs), wheat sprouts, common nettle (Urtica dioica). In edible mushrooms zinc can be found from 25 to 200 mg/kg of dry weight. Best source of zinc is common puffball (Lycoperdon perlatum), for which content of zinc from 150 to 200 mg/kg of dry weight could be observed. A good source of this element are also: Field mushroom (Agaricus campestris), King bolete (Boletus edulis), Parasol mushroom (Macrolepiota procera), Bay bolete (Boletus badius) or Birch bolete (Leccinum scabrum). In edible mushrooms magnesium can be found in amounts ranging from 25 to 125 mg/kg of dry weight. The best sources of this element are: Boletus edulis, in which magnesium can be found from 75 to 125 mg/kg of dry weight, and Macrolepiota procera [57].

Conclusions

Prophylaxis consisting of constant supplementation of vital for health substances can be a base to keep the organism in good condition and prevent diseases occurrence. Daily diet, which can be a source of substances and elements that reduce the symptoms of depression, is also important.

Described raw materials and natural formulations may be important in prophylaxis and in prevention of mood disorders. Many of these materials require further studies, and are not a substitute for the treatment of clinical cases. The application and the possible selection of products containing raw materials primarily standardized on the active ingredients should be determined by a specialist doctor.

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