REVIEW ARTICLE

Psychoactive plants used in designer drugs as a threat to public health

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Summary

Based on epidemiologic surveys conducted in 2007–2013, an increase in the consumption of psychoactive substances has been observed. This growth is noticeable in Europe and in Poland. With the ‘designer drugs’ launch on the market, which ingredients were not placed on the list of controlled substances in the Misuse of Drugs Act, a rise in the number and diversity of psychoactive agents and mixtures was noticed, used to achieve a different state of mind. Thus, the threat to the health and lives of people who use them has grown. In this paper, the authors describe the phenomenon of the use of plant psychoactive substances, paying attention to young people who experiment with new narcotics. This
article also discusses the mode of action and side effects of plant materials proscribed under the Mis-use of Drugs Act in Poland.

Key words: designer drugs, plant materials, drugs, adolescents

INTRODUCTION

Anthropological studies concerning preliterate societies have shown that psychoactive substances have been used for ages. On the individual level, they achieve emotional relief, resolve anxiety or phobia, reduce the physical symptoms, stimulate despite fatigue, or help forget daily problems. In a social context, psychoactive substances are used for many rituals and as a symbol in religious ceremonies [1]. In recent years, Internet plays a crucial role in disseminating information and getting access to drugs. In population survey on 15–24-year-olds in the UE countries 61% of respondents said that they would use the Internet to learn more about drugs and their application. Except Internet, the knowledge about drugs comes from: friends (35%), medical staff (24%), family (27%) and school (25%) [2]. Adolescents are special group vulnerable to risky behaviors; one of them is the use of psychoactive substances. They are often influenced by peer group and environmental factors. Other factors that increase the risk of substance abuse are school problems, class absence, poor school performance, low self-esteem, difficulties in social adaptation, family and behavioral problems. Due to the lack of mechanisms helping cope with difficult situations poor life experience, young people think that drugs are a solution of their problems. Psychoactive substances are also used to reduce boredom or to increase activity [3, 4].

The most commonly used drugs in Poland are preparations made of various parts of the cannabis (Cannabis sativa). Its psychoactive component is tetrahydrocannabinol (THC) [5]. In 2011 compared to 2007 a significant increase in the use of cannabis and other inhaled drugs was noted. The proportion of 15- and 16-year-old Polish schoolchildren who used cannabis at least once was 23%, for inhaled drugs it was 8%, while the average for European countries amounted to 17% and 9%, respectively. Poland is often close to European average in terms of the eight variables determining the consumption of psychoactive substances. For at least one use of illicit drugs, which include cannabis, amphetamines, cocaine, crack, ecstasy, LSD, heroin, GHB or other hallucinogenic
substances in case of boys there was 30% and 20% positive responds, while for girls it was 20% and 15%, respectively for Polish and European teenagers [6].

DESIGNER DRUGS IN POLAND

With the introduction of the substitutes for illegal drugs (natural highs, legal highs, designer drugs, highs) at Polish market, the use of psychoactive substances has grown among young people [7]. Designer drug is the common name of various types of psychoactive substances or their mixes of hallucinogenic, stimulating or relaxing type of action. They are mixtures of plant materials and/or synthetic substances which are supposed to produce effects similar to those of prohibited drugs. Designer drugs were supposed to be legal alternatives. In Poland, by 2010 designer drugs were available as “collection products” in stationary shops in major cities. Till the 2009 prohibited raw plant materials and its preparations in Poland were only cannabis (Cannabis sativa), opium poppy (Papaver somniferum) and coca leaves (Erythroxylum coca). Table 1 summarizes raw plant materials, added in 2009 due to amendment of Act on Counteracting Drug Addiction, to the I-N list of drugs that may be used only for medical, industrial or research purposes after the Main Pharmaceutical Inspector approval [8, 9]. It contains information about the main psychoactive substances, the mode of action and side effects after use of plant materials.

Currently, there is a ban on designer drugs sale in Poland. In the second half of 2010 there was an increase of the number of medical interventions and hospitalizations after use of legal highs, so in October it reached the number of 258 such cases. Due to these facts the Main Sanitary Inspector decided to close shops, warehouses and places where ‘highs’ were produced. The effectiveness of actions taken is proved by a very rapid decrease in the number of poisonings [10]. Although they are prohibited, psychoactive plant mixes are available in the Internet. Such products are accompanied with annotation that they are not suitable for consumption. They are described as: an imitation of grill kindling, insecticides, fertilizers, anti-mosquito agents, paint drying accelerators, blends of herbs and aromas, bath or wash salts. Based on research conducted in Poland among young people in 2008, 2010 and 2013 3.5%, 11.4% and 5.2% of respondents, respectively, admitted that they were using designer drugs. In case of use within 12 months the figures were 2.6%, 7.2% and 2%, while for 30-day period these values are 1.5%, 1.1% and 1% [11]. These results show clear decrease in the consumption of designer drugs between 2010 and 2013.
Apparent reduction in these numbers is associated with the amendment of Misuse of Drugs Act in 2009.

ILLEGAL PLANT SPECIES DESCRIPTION

Hawaiian Baby Woodrose (*Argyreia nervosa, Convolvulaceae*) is widely distributed in tropical regions of the world, grows in India and Bangladesh. Traditionally, it was used in gonorrhoea, chronic ulcers, strangury, gleet [12], bronchitis, tuberculosis, arthritis and nervousness [13]. Jeet et al. [12] have shown that methanol and ethyl acetate extracts of whole aerial part of *Argyreia nervosa* have antipyretic activity in animal model, but the exact active principle responsible for this effect is still unknown. Subramoniam et al. [14] investigated the aphrodisiac property of its flower and leaf alcohol extracts. Their study results have shown statistically significant increase of observed sexual behaviour in male mice. Pharmacological studies of *Argyreia nervosa* extracts indicated that it can be used also in gastric ulceration and has anti-inflammatory, antiarthritic, antimicrobial, immunomodulatory and antifilarial activities [15, 16]. Due to the content of psychoactive compounds, in South American cultures Hawaiian Baby Woodrose has been used for centuries in shamanistic rituals [17]. Its seeds contain various lysergic acid derivatives and ergoline alkaloids [18, 19]. Ergine-lysergic acid amide binds to the 5-HT2A receptor (serotonin receptor family) and gives effects similar to LSD (lysergic acid) [13]. Seeds are eaten whole, crushed or consumed as an extract after soaking in water [20]. The main symptoms after ingestion are: visual and auditory hallucinations, anxiety, and euphoria [17, 21]. Vegetative side effects range from nausea, vertigo, hypertension, tachycardia, tachypnea to mydriasis [13]. Kremer et al. [17] described small human study where seeds of *Argyreia nervosa* were employed as a source of LSA. Unfortunately, the study was canceled due to severe side effects which appeared in participants. Many symptoms were observed, e.g. nausea, fatigue, hand tremors, cardiovascular dysregulation and psychosis-like state. In addition to abovementioned symptoms, recreational users also describe effects such as: abdominal pain, nausea, persecutory delusions, depressive mood. Some positive emotions were also experienced: euphoria, happiness, the feeling of beauty and delight [21].

*Banisteriopsis caapi* (*Malpighiaceae*) is native for north parts of South and Central America. Its woody vines are an ingredient of the popular psychoactive drink, Ayahuasca.
[22], which is used for prophecy and as a sacrament in South America. Main active substances (MAOIs) of Banisteriopsis caapi are tetrahydroharmine (THH), harmaline and harmine [23]. To achieve psychoactive effect, Caapi is used with plants containing N,N-dimethyltryptamine (DMT). As a result, DMT psychoactive activities are facilitated with harmala alkaloids which work through inhibition of monoamine oxidase (MAO) in central nervous system and liver. Use of DMT causes strong visual effects, euphoria and hallucinations [24]. After ingestion of ayahuasca also effects such as: nausea, changes in visual and auditory perception, psychological introspection, stimulation and blood pressure increase were reported [22]. Serrano-Dueñas et al. [25] reported significant improvement in motor functions of the patients in trial of Banisteriopsis caapi extracts, however, tremor was not improved and in some patients were exacerbated. All patients experienced nausea or vomiting, but these side effects were much less severe than those experienced by users of complete ayahuasca drink. Few years later, Samoylenko et al. [23] showed that Caapi demonstrated significant inhibitory and antioxidant activities, which are relevant to the prevention of neurological disorders, so it has a potential therapeutic value for the treatment of Parkinson’s disease.

*Calea zacatechichi* (syn. *Calea ternifolia*, Asteraceae) is indigenous plant of Mexico. It is used in many illnesses, such as rheumatism, oedema, respiratory tract disorders, cold fever, painful limbs [26]. It is administered in infusions made of dried leaves and stalks [27]. Due to its oneirogenic properties, *Calea* was originally used to induce lucid dreams, increase dreaming and to produce life-like dream experiences [28, 29]. It is rich in isoprenoids, mainly bicyclic sesquiterpenes [27]. Segura-Cobos et al. [26] proved that methanol extracts from *Calea zacatechichi* leaves have anti-inflammatory and perception of pain reducing properties. However, compounds responsible for psychoactive activity acting on the receptors of the central nervous system have not been identified yet. It is suspected that this plant contains small amounts of alkaloids [27]. After ingestion of large doses of *Calea* side effects, e.g. salivation, ataxia, retching and vomiting are observed [29].

*Khat* (*Catha edulis*), qat, chat, qaad, catha [30] – belongs to *Celastraceae* family. Chewing khat leaves and bark is common in East Africa and Arabian Peninsula; it is valued mostly for stimulant effects, reduction of fatigue and enhancing concentration [31]. *Catha edulis* is also used as a socialising and recreational drug. The main active compounds are cathine and cathinone, chemically similar to amphetamine [30, 32]. Cathinone works by increasing the amount of neurotransmitter – dopamine [33, 34]. The phenylpropylamine composition of khat varies between countries and regions of origin.
Frequent adverse effects of khat consumption are reactive depression, anxiety and irritability, induction of dependence [35]. There are documented physical withdrawal symptoms: lassitude, anergia, nightmares, slight trembling, depressive disorder, sedation and hypotension [30]. Other short-term and long-term side effects of chewing khat are dry mouth, blurred vision, blood pressure increase, periodontal disease, stomatitis, gastritis, pre-cancerous lesions, malnutrition, constipation, hallucinations. Also in several case studies psychotic states [30, 32] and liver failures associated with chronic khat use [35] have been described.

San Pedro (*Echinopsis pachanoi*, Cactaceae) and Peruvian Torch (*Echinopsis peruviana* syn. *Trichocereus peruvians*, Cactaceae) are columnar cacti native to the western slope of the Andes in Peru, Ecuador and Bolivia, they grow at an altitude of 2000–3000 m above sea level [36]. There are not many scientific reports describing these plants, their use and side effects. Their preparation includes slicing and boiling of cactus stems. Usually they are ingested in form of decoction [37]. In South America, San Pedro has an important cultural history. Since pre-Columbian times, due to its psychomimetic properties, it has been used by Indians during their religious ceremonies and healing rituals to treat physical, mental, emotional and supernatural diseases [36, 37]. The main biologically active substance both in Peruvian Torch and San Pedro, is mescaline, which is an agonist of 5-HT2A serotonin receptor [38]. Mescaline has stimulative and hallucinogenic properties. *Echinopsis pachanoi* also contains traces of tyramine, hordenine, 3-methoxytyramine, 3,4-dimethoxy-β-phenethylamine, 3,4-dimethoxy-4-hydroxy-β-phenethylamine and anhalonidine [39]. But the side effects of San Pedro and Peruvian Torch use are assigned to mescaline, and they are, among others: increased heart rate and blood pressure, sleeplessness and tremors, convulsions, depression, anxiety, psychosis [40].

Wild dagga, lion’s tail (*Leonotis leonurus*, Lamiaceae) is a plant native in South Africa, sometimes used as a cannabis substitute. Its leaves have traditionally been smoked for the relief of epilepsy. Infusions and decoctions were used to treat coughs, colds, influenza, bronchitis, delayed menstruation, constipation, intestinal worms, high blood pressure and headaches. Externally it was used to treat boils, skin disease, itching and muscular cramps [41, 42]. Pharmacological research suggested that *L. leonurus* water and lipid extracts possess anti-inflammatory, antinociceptive, anticonvulsant, antibacterial, antioxidant, anthelmintic and hypoglycemic properties [43]. Wild dagga extracts contain tannins, quinones, saponins, labdane lactones, triterpene steroids [44], alkaloids (leonitin,
leonurine) [45] and diterpenoid lactone – marrubiin [46]. Psychoactive pharmacological activity of abovementioned alkaloids is still unknown. Wild dagga gives short-term effects such as relaxation, fatigue reduction and euphoric marijuana-like experience [40]. Frequent use causes addiction comparable to nicotine. It disrupts consciousness and perception, at higher doses nausea, vomiting and muscle tension may appear [45].

Jurema-Preta (Mimosa tenuiflora, syn. Mimosa hostilis, Mimosaceae) naturally grows in North part of South America and in Mexico. It has been traditionally used by the Brazilian Indians for curing infections, inflammations against bronchitis, coughs, headache, external ulcers and also for divination [47, 48]. Pharmacological studies showed that M. tenuiflora extracts show antimicrobial, antiplasmolytic, anti-inflammatory, hemolytic and wound healing activities [47, 49]. It contains diverse classes of secondary metabolites – indole alkaloids, tannins, chalcones, steroids, saponins and flavonoids [48]. There are reports of teratogenic action of Mimosa tenuiflora for ruminants and rats. Craniofacial anomalies and skeletal malformations are observed in newborn animals [50, 51]. Stem bark contains main psychoactive compounds – yuremamine and DMT (dimethyltryptamine). DMT induces psychoactive effects with monoamine oxidase inhibitors (MAOIs). It influences 5-HT, D1, α1 and α2-adrenergic receptors [52]. Jurema root or stem bark, together with MAOIs, is one of the ritual Ajuca (jurema wine) drink ingredients [47, 53]. The effects of Jurema use are: anxiety, dizziness, hallucinations, perception changes [47].

Kratom, Kakuam, Kraton, Thom, Ithang, Biak-Biak, Ketum (Mitragyna speciosa, Rubiaceae) grows in Thailand, Malaysia, Laos, Cambodia and in the East and West Africa and India [54]. Its leaves are known as kratom, ketum or kratum. They have been used as opium substitute, also in treating drug addiction, and as a stimulant [55]. In traditional medicine it is used to treat cough, diarrhea, hypertension and in pain alleviation [56]. Primary ingredients responsible for psychoactive effect are alkaloids – mitragynine and 7-hydroxymitragynine [55, 57, 58]. Their pharmacological mechanism is similar to that of salvinorin A, so they are a partial agonists of opioid receptors [55]. In lower doses, kratom works as a stimulant and in higher doses has a calming effect [52, 58]. After long-term use side effects including decreased diuresis, loss of appetite, darken skin, dry mouth and constipation are observed. There is also speculated that it causes impairment in hepatic function and liver cell injury [54].

Blue lotus, blue lily, Egyptian lotus (Nymphaea caerulea, Nymphaeaceae) is a water plant native for East Africa and Asia. It was used in folk medicine as a sedative, detoxicant
and aphrodisiac. It is also applied in ayurvedic medicine for a variety of conditions, such as dyspepsia, diarrhea, fevers, urinary problems and heart palpitations [59]. The lily flowers were used in ancient civilizations of Egyptians and Mayans as a ritual plant to reach euphoria and ecstasy [60]. This plant contains various classes of compounds such as alkaloids, tannins, phenolic acids and flavonoids [61]. The main substances responsible for psychoactive properties of blue lotus are alkaloids – nuciferine and aporphine [62]. They are dopamine receptor agonists [52]. Active ingredients of *Nymphaea caerulea* can affect heart rate and blood pressure, but there are no available scientific reports concerning side effects of this plant [52].

Wild rue (*Peganum harmala, Nitrariaceae*) (syn. African rue, rue weed, Syrian rue, Harmal, isband, ozallaik, ruin weed, steppenraute) is native to Northern Africa, the Middle East, Pakistan, India and Mediterranean Basin [63]. Various parts of *P. harmala* have been used in folk medicine to treat cardiac, gastrointestinal diseases, in rheumatism, fever, ulcers and also in diabetes or as a pain reliever [64]. Its main active compounds are β-carboline alkaloids: harmaline and harmine, harmalol and harmane [65]. All of them are a monoamine oxidase inhibitors (MAOIs). The alkaloids in the seeds have antibacterial, vasorelaxant, antihemosporidian, anticancer, antinociceptive, antitumor and antiprotozoal properties [66]. It has been proven that β-carbolines from *P. harmala* interact with opioid, dopamine, GABA, 5-hydroxytryptamine, benzodiazepine and imidazoline receptors, so they induce many pharmacological effects [64]. Wild rue is also one of the constituents of Ayahuasca, a hallucinogenic beverage ingested in rituals by the Amazonian tribes. Short term effects of its use are stress reduction, stimulation and euphoria [40]. Possible side effects after overdose or ingestion for medicinal use or as a recreational product are: paralysis, hypothermia, bradycardia, hallucinations, agitation, locomotor ataxia, vomiting, nausea, convulsions, coma, low blood pressure [63, 67]. *Peganum harmala* is also a teratogen and causes miscarriages [64].

Kava Kava, awa, yaqona (*Piper methysticum, Piperaceae*) is a native plant of the South Pacific [68]. Traditionally, its water roots infusion has been used for the treatment of gonorrhoea, rheumatism, bronchitis, asthma, stomachaches, headaches, insomnia, anxiety [68, 69] and also in religious, social and cultural purposes [70]. Main psychoactive compounds of the roots are kavalactones: desmethoxyyangonin, dihydrokavain, yangonin, kavain, dihydromethysticin and methysticin [69, 71]. The effects after kava use include mild euphoria and sociability. Small doses produce stimulation while larger ones cause muscle relaxation, incoordination and somnolence [72]. The mode of action of *Piper*
methysticum ingredients are through their ability to increase GABA activity [73]. Side effect involve: accommodation disorder, allergic reactions, liver failure, skin reactions, seizures [69, 74].

Psychotria viridis, Rubiaceae is native plant to Amazon, contains indol alkaloids, mainly DMT, which is responsible for psychoactive properties of the plant. It is one of the admixtures of the Ayahuasca drink, also known as Yage, Hoasca, Daime [22], Caapi, Pinde, Natema or Yaje [23]. Along with plants that have activity of monoamine oxidase inhibitors (usually it is Banisteriopsis caapi), it gives strong psychoactive effects such as visuals, euphoria and hallucinations [75]. This drink is the core of spiritual doctrines of many religious groups in South America [24]. Psychoactive properties of Psychotria viridis are a result of the presence of DMT, consequently, the mechanism of action is similar to the Mimosa tenuiflora.

Ololiuhqui, Rivea corymbosa, syn. Turbina corymbosa, Convolvulaceae grows naturally in Mexico and South America [76]. Its seeds contain hallucinogenic substance – ergine (LSA-lysergic acid amide), which is the non-alkylated amide-analogue of LSD. Ergine is a partial agonist of 5-HT2A receptor and after ingestion it gives psychoactive effects similar to LSD [77]. There are only few scientific reports on the human consumption of seeds containing LSA. Side effects are comparable to those observed after ingestion of Argyreia nervosa; some patients can experience hallucination, derealization, memory loss, anxiety, suicidal ideation and also tachycardia, hypertension, pupil dilation, flushing, polyuria, nausea [20].

Diviner’s Sage, Mystic Sage, Sally D, Magic Mint (Salvia divinorum, Lamiaceae) occurs naturally in Mexico [78]. It has been used traditionally in divination rituals and also to treat many conditions including anemia, headache, rheumatism, diarrhea [79]. Its principal active component (salvinorin A) is a highly selective agonist of κ-opioid receptor [80]. Salvia is appealing to recreational users because of intense hallucinations and relatively short duration of effects [79]. The potential harm and degree of the addiction to recreational use of Salvia is still unclear. The most common symptoms are confusion, dizziness, flushed sensation, tachycardia and hypertension [78].

Iboga, eboga (Tabernanthe iboga, Apocynaceae) is a plant native to West Africa. Its roots are chewed to combat fatigue and to keep hunters awake [72]. In Gabon, they have been used in the initiation rites and it is believed that it enables them to contact with spirits of their ancestors [76]. Iboga main hallucinogenic compound is ibogaine, which is also used for opioid detoxification in humans [81]. It has been shown that it has an activity of
serotonin transporter (SERT) inhibitor [82]. Effects of Tabernanthe iboga use are dose-dependent; in lower doses it is a stimulant, in higher doses it has sedative properties. It also causes visualizations and euphory [52]. It can cause serious side effects, such as tremos, ataxia, cardiac toxicity and even fatalities [72].

CONCLUSIONS

Designer drugs are a significant problem of public health, particularly in the prevention of drug addiction. As we can see, psychoactive substances are not safe and non-addictive, they threaten lives and health. The analysis of many studies made it possible to know more about plant materials in natural designer drugs and therefore to conclude that many of them are strongly toxic. Their use can lead to serious damage of central nervous system and even to death. Still there are few formal clinical reports describing the effects of the use of designer drugs. There is lack of reliable and complete information concerning overdose or long-term effects of their use. The specificity of adolescence, unlimited access to the Internet and to drugs available online make young people particularly vulnerable to experiments with new substances. Psychoactive compounds are a direct threat to their normal development and health. Due to the big scale of the risks associated with drugs, there is a need to launch prevention projects and education programs amongst the adolescents.

REFERENCES


ROŚLINY PSYCHOAKTYWNE W DOPALACZACH JAKO ZAGROŻENIE DLA ZDROWIA PUBLICZNEGO

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Streszczenie

Na podstawie badań epidemiologicznych w Polsce i Europie w latach 2007–2013 zaobserwowano wzrost konsumpcji środków psychoaktywnych. Wraz z wprowadzeniem na rynek tzw. dopalaczy, których składniki do 2009 r. nie znajdowały się na liście substancji kontrolowanych przepisami Ustawy o przeciwdziałaniu narkomanii, zwiększyła się liczba i różnorodność stosowanych substancji psychoaktywnych oraz ich mieszanek. Tym samym też wzrosło zagrożenie dla zdrowia i życia osób je zażywających. W niniejszej pracy autorzy omawiają zjawisko zażywania substancji
psychoaktywnych pochodzenia roślinnego ze zwróceniem uwagi na jego występowanie wśród młodych, chętnie eksperymentującej z nowymi narkotykami. Artykuł również omawia sposób działania oraz działania niepożądane zażywania produktów zawierających surowce roślinne, które zostały zdelegalizowane na mocy ustawy o przeciwdziałaniu narkomanii w Polsce.

**Słowa kluczowe:** dopalacze, surowce roślinne, substancje psychoaktywne, młodzież

**Table 1.**

Main psychoactive substances in designer drugs, their pharmacological activity and possible side effects

<table>
<thead>
<tr>
<th>Plant species</th>
<th>Main psychoactive substances</th>
<th>Pharmacological activity</th>
<th>Possible side effects [according to O'Mahony CS. 2010]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argyreia nervosa</td>
<td>lysergic acid derivatives</td>
<td>binds to 5-HT2A receptor, similar to LSD [40]</td>
<td>anxiety, confusion, convulsions, hallucinations, dizziness, liver problems, miscarriage, nausea, panic, paranoia, fear, vomiting, exhaustion, large doses may result in necrosis of the tissue</td>
</tr>
<tr>
<td>Banisteriopsis caapi</td>
<td>THH, harmaline, harmine [15, 47]</td>
<td>MAOI, facilitates DMT effects [46]</td>
<td>convulsions, difficulty breathing, laxative, trembling, lower heart rate, paralysis, strong hallucinations, dizziness, nausea, vomiting</td>
</tr>
<tr>
<td>Calea zacatechichi</td>
<td>sesquiterpene lactones [50]</td>
<td>unknown</td>
<td>decrease of REM sleep, difficulty in bringing events to mind, drowsy, in large doses – hallucinogenic, retching</td>
</tr>
<tr>
<td>Catha edulis</td>
<td>cathinone cathine [53, 54]</td>
<td>stimulates release of neurotransmitters [55]</td>
<td>anxiety, aggressiveness, decreased cardiovascular capacity, dizziness, drowsiness, epigastric pain, impotence, liver damage, manic behaviours</td>
</tr>
<tr>
<td>Echinopsis pachanoi, Trichocereus</td>
<td>mescaline [57, 58]</td>
<td>agonist of 5-HT2A receptor [21]</td>
<td>fever, dizziness, tremors, insomnia, nausea, chills, anxiety, feelings of terror, vomiting</td>
</tr>
<tr>
<td>Leonotis leonurus</td>
<td>leonitin, leonurine [64]</td>
<td>unknown</td>
<td>diarrhea, dizziness, nausea, sweat inducing</td>
</tr>
<tr>
<td>Mimosa tenuiflora</td>
<td>DMT [24]</td>
<td>5-HT, D1, α1, α2 – adrenergic receptors agonist [23]</td>
<td>stomach cramps, vomiting</td>
</tr>
<tr>
<td>Mitragyna speciosa</td>
<td>mitragynine, 7-hydroxymitragynine [75]</td>
<td>opioid receptor partial agonists [72]</td>
<td>constipation, dysphoria, nausea, psychological addiction, vomiting</td>
</tr>
<tr>
<td>Nymphaea caerulea</td>
<td>nuciferine, aporphine [28]</td>
<td>dopaminergic receptor agonist [23]</td>
<td>muscle tremors, nausea</td>
</tr>
<tr>
<td>Peganum harmala</td>
<td>harmaline, harmine [29]</td>
<td>MAOI [80]</td>
<td>convulsions, nausea, stomach cramps, dizziness, vomiting, body tremors, hallucinations, increased bradycardia, neurotoxic, phototoxic</td>
</tr>
<tr>
<td>Piper methysticum</td>
<td>kavalactones [31]</td>
<td>increasing GABA activity [32]</td>
<td>dizziness, drowsiness, drying of skin, gastrointestinal discomfort, headache, liver damage, muscle weakness, nausea, tremors, visual impairment</td>
</tr>
<tr>
<td>Psychotria viridis</td>
<td>DMT [47]</td>
<td>5-HT, D1, α1, α2 – adrenergic receptors agonist [47]</td>
<td>nausea, vomiting</td>
</tr>
<tr>
<td>Rivea corymbosa</td>
<td>ergine [77]</td>
<td>partial agonist of the 5-HT2A receptor [52]</td>
<td>miscarriage, diarrhea, hallucinations, carcinogenic, liver problems, nausea, vomiting</td>
</tr>
<tr>
<td>Salvia divinorum</td>
<td>salvinorin A [80]</td>
<td>kappa opioid receptor agonist [80]</td>
<td>dissociation, dizziness, fear, panic, inability to maintain balance, nausea, short term memory impairment, slurred speech, confusion, paranoia</td>
</tr>
<tr>
<td>Tabernanthe iboga</td>
<td>ibogain [81]</td>
<td>serotonin transporter inhibitor [82]</td>
<td>ataxia, nausea, vomiting</td>
</tr>
</tbody>
</table>