

REVIEW PAPER

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

AGNIESZKA RONDZISTY¹, KAROLINA DZIEKAN^{2*}, ALEKSANDRA KOWALSKA²

¹Department of Humanities in Medicine
Pomeranian Medical University
Chłapowskiego 11
70-103 Szczecin, Poland

²Department of Stem Cells and Regenerative Medicine
Institute of Natural Fibers and Medicinal Plants
Kolejowa 2
62-064 Plewiska, Poland

*corresponding author: e-mail: karolina.dzieskan@iwnirz.pl

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 Misuse 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 help to

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.

Table 1.

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

Plant species	Main psychoactive substances	Pharmacological activity	Possible side effects [according to O'Mahony CS. 2010]
<i>Argyrea nervosa</i> (Convolvulaceae)	lysergic acid derivatives [12, 13]	binds to 5-HT _{2A} receptor, similar to LSD [40]	anxiety, confusion, convulsions, hallucinations, dizziness, liver problems, miscarriage, nausea, panic, paranoia, fear, vomiting, exhaustion, large doses may result in necrosis of the tissue
<i>Banisteriopsis caapi</i> (Malpighiaceae)	THH, harmaline, harmine [15, 47]	MAOI, facilitates DMT effects [46]	convulsions, difficulty breathing, laxative, trembling, lower heart rate, paralysis, strong hallucinations, dizziness, nausea, vomiting
<i>Calea zacatechichi</i> (Asteraceae)	sesquiterpene lactones [50]	unknown	decrease of REM sleep, difficulty in bringing events to mind, drowsy, in large doses – hallucinogenic, retching
<i>Catha edulis</i> (Celastraceae)	cathinone cathine [53, 54]	stimulates release of neurotransmitters [55]	anxiety, aggressiveness, decreased cardiovascular capacity, dizziness, drowsiness, epigastric pain, impotence, liver damage, manic behaviours
<i>Echinopsis pachanoi</i> , <i>Trichocereus peruvianus</i> (Cactaceae)	mescaline [57, 58]	agonist of 5-HT _{2A} receptor [21]	fever, dizziness, tremors, insomnia, nausea, chills, anxiety, feelings of terror, vomiting
<i>Leonotis leonurus</i> (Lamiaceae)	leonitin, leonurine [64]	unknown	diarrhea, dizziness, nausea, sweat inducing
<i>Mimosa tenuiflora</i> (Mimosaceae)	DMT [24]	5-HT, D1, α 1, α 2 – adrenergic receptors agonist [23]	stomach cramps, vomiting
<i>Mitragyna speciosa</i> (Rubiaceae)	mitragynine, 7-hydroxymitragynine [75]	opioid receptor partial agonists [72]	constipation, dysphoria, nausea, psychological addiction, vomiting
<i>Nymphaea caerulea</i> (Nymphaeaceae)	nuciferine, aporphine [28]	dopaminergic receptor agonist [23]	muscle tremors, nausea
<i>Peganum harmala</i> (Nitrariaceae)	harmaline, harmine [29]	MAOI [80]	convulsions, nausea, stomach cramps, dizziness, vomiting, body tremors, hallucinations, increased bradycardia, neurotoxic, phototoxic
<i>Piper methysticum</i> (Piperaceae)	kavalactones [31]	increasing GABA activity [32]	dizziness, drowsiness, drying of skin, gastrointestinal discomfort, headache, liver damage, muscle weakness, nausea, tremors, visual impairment
<i>Psychotria viridis</i> (Rubiaceae)	DMT [47]	5-HT, D1, α 1, α 2 – adrenergic receptors agonist [47]	nausea, vomiting
<i>Rivea corymbosa</i> (Convolvulaceae)	ergine [77]	partial agonist of the 5-HT _{2A} receptor [52]	miscarriage, diarrhea, hallucinations, carcinogenic, liver problems, nausea, vomiting
<i>Salvia divinorum</i> (Lamiaceae)	salvinorin A [80]	kappa opioid receptor agonist [80]	dissociation, dizziness, fear, panic, inability to maintain balance, nausea, short term memory impairment, slurred speech, confusion, paranoia
<i>Tabernanthe iboga</i> (Apocynaceae)	ibogain [81]	serotonin transporter inhibitor [82]	ataxia, nausea, vomiting

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 on 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* Burm. f. Bojer, *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 *A. 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 *A. nervosa* extracts indicated that it can be used also in gastric ulceration and has antiinflammatory, 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-HT_{2A} 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 *A. 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 [17]. 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 (Spruce ex Griseb, Morton (*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 *B. 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 *B. 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 Kunth (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 *C. 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* (Vahl) Forssk. ex Endl.), 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]. *C. 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* (Britton & Rose), *Cactaceae*) and Peruvian Torch (*Echinopsis peruviana* syn. *Trichocereus peruvians* (Britton & Rose) Friedrich & G.D. Rowley, *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-HT_{2A} serotonin receptor [38]. Mescaline has stimulative and hallucinogenic properties. *E. 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* (L.) R. BR., *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* (Willd.) Poir., 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, antiplasmodic, 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 *M. 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, $\alpha 1$ and $\alpha 2$ -adrenergic receptors [52]. Juremas 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* (Korth.) Havil., *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* Sav., *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 *N. 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* L., *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 harmene [65]. All of them are 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* G. Forst., *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: desmethoxyangonin, 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 *P. 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 Ruiz & Pav. (*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*.

Ololihuiqui (*Rivea corymbosa* (L.) Raf., 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-HT_{2A} 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* Epling & Jativa, *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* (L.) Nutt., *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 *T. iboga* use are dose-dependent; in lower doses it is a stimulant, in higher doses it has sedative properties. It also causes visualizations and euphoria [52]. It can cause serious side effects, such as tremors, 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

1. Westermeyer J. Historical and social context of psychoactive substance use disorders. In: Frances RJ, Miller SI, Mack AH (eds.). Clinical textbook of addictive disorders. 3rd ed. New York. The Guilford Press, 2005:16-34.
2. European Commission (2008). Eurobarometer: young people and drugs among 15–24 year olds. Analytical report. Dublin, Ireland (http://ec.europa.eu/public_opinion/flash/fl_233_en.pdf), accessed 13.06.2008.
3. Boys A, Marsden J, Strang J. Understanding reasons for drug use amongst young people: a functional perspective. Health Educ Res 2001; 16(4):457-469.
4. Wang SH, Chen WC, Lew-Ting CY, Chen CY, Chen WJ. Running away experience and psychoactive substance use among adolescents in Taiwan: multi-city street outreach survey. BMC Public Health 2010; 10:29. doi:10.1186/1471-2458-10-29.
5. Stawicka E. Nadużywanie substancji psychoaktywnych przez dzieci i młodzież. Post N Med 2006; 6:333-340.
6. Hibell B, Guttormsson U, Ahlström S, Balakireva O, Bjarnason T, Kokkevi A et al. Substance use among students in 36 European countries. The 2011 ESPAD Report 2012. www.espad.org/uploads/espad_reports/2011/the_2011_espad_report_full_2012_10_29.pdf.
7. Malczewski A, Misiurek A, Bukowska, B, Chojecki D, Jabłoński P, Kidawa M et al. National Report 2013, Poland: new developments, trends and in-depth information on selected issues. Krajowe Biuro ds. Przeciwdziałania Narkomanii.
8. Ustawa z dnia 29 lipca 2005 r. o przeciwdziałaniu narkomanii, Dz.U. z 2005 r. Nr 179, poz. 1485.
9. Ustawa z dnia 20 marca 2009 r. o zmianie ustawy o przeciwdziałaniu narkomanii, Dz.U. z 2009 r. Nr 63, poz. 520.
10. Główny Inspektorat Sanitarny, Departament Nadzoru nad Środkami Zastępczymi. Raport Głównego Inspektora Sanitarnego w sprawie środków zastępczych – trzy lata zwalczania dopalaczy w Polsce, 2013.
11. Malczewski A. Młodzież a substancje psychoaktywne. In: Raport CBOS – Młodzież 2013. Warszawa 2014.
12. Jeet K, Tomar S, Thakur N. Antipyretic activity of whole aerial part from *Argyrea nervosa*. Int J Pharm Pharm Sci 2012; 4 (4):76-77.
13. Paulke A, Kremer Ch, Wunder C, Achenbach J, Djahanschiri B, Elias A et al. *Argyrea nervosa* (Burm. f.): receptor profiling of lysergic acid amide and other potential psychedelic LSD-like compounds by computational and binding assay approaches. J Ethnopharmacol 2013; 148 (2):492-497.
14. Subramoniam A, Madhavachandran V, Ravi K, Anuja VS. Aphrodisiac property of the elephant creeper *Argyrea nervosa*. J Endocrinol Reprod 2007; 11(2):82-85.
15. Joseph A, Mathew S, Skaria BP, Sheeja EC. Medicinal uses and biological activities of *Argyrea speciosa* sweet (Hawaiian Baby Woodrose) – an overview. Indian J Nat Prod Res 2011; 2(3):286-291.
16. Padhi M, Mahapatra S, Panda J, Mishra NK. Traditional uses and phytopharmacological aspects of *Argyrea nervosa*. J Adv Pharm Res 2013; 4(1):23-32.
17. Kremer C, Paulke A., Wunder C, Toennes SW. Variable adverse effects in subjects after ingestion of equal doses of *Argyrea nervosa* seeds. For Sci Intern 2012; 214:e6-e8.
18. Bojer EW, Chao JM, Marderosian AH. Ergoline alkaloidal constituents of Hawaiian baby woodrose, *Argyrea nervosa* (Burm. f.). J Pharm Sc. 1973; 62:588-591.
19. Borsutzky M, Passie T, Paetzold W, Emrich HM, Schneider U. Hawaiian baby woodrose: (Psycho-) pharmacological effects of the seeds of *Argyrea nervosa*. A case-orientated demonstration. Nervenarzt 2002; 73(9):892-896.
20. Klinke HB, Müller IB, Steffenrud S, Dahl-SØrensen R. Two cases of lysergamide intoxication by ingestion of seeds from Hawaiian Baby Woodrose. For Sci Int 2010; 197:e1–e5.
21. Juszcak GR, Swiergiel AH. Recreational use of D-lysergamide from the seeds of *Argyrea nervosa*, *Ipomoea tricolor*, *Ipomoea violacea*, and *Ipomoea purpurea* in Poland. J Psych Drugs 2013; 45(1):79-93.
22. Sklerov J, Tevine B, Moore K.A, King T, Fowler D. Fatal intoxication following the ingestion of 5-methoxy-N,N-dimethyltryptamine in an Ayahuasca preparation. J Anal Toxicol 2005; 29(8):838-841.

23. Samoylenko V, Rahmana MM, Tekwani BL, Tripathi LM, Wang YH, Khan SI et al. *Banisteriopsis caapi*, a unique combination of MAO inhibitory and antioxidative constituents for the activities relevant to neurodegenerative disorders and Parkinson's disease. *J Ethnopharmacol* 2010; 127:357-367.
24. Callaway JC, Glacus S, Brito MD, Neves ES. Phytochemical analyses of *Banisteriopsis caapi* and *Psychotria viridis*. *J Psychoactive Drugs* 2005; 37(2):145-150.
25. Serrano-Dueñas M, Cardozo-Pelaez F, Sánchez-Ramos JR. Effects of *Banisteriopsis caapi* extract on Parkinson's disease. *Sci Rev Altern Med* 2001; 5(3):139-134.
26. Segura-Cobos D, Venegas-Flores H, Baiza-Gutman LA, Vázquez-Cruz B. Antinociceptive and anti-inflammatory effects of the methanol extract of *Calea zacatechichi* leaves and its fractions. *Pharmacologyonline* 2010; 2:1100-1110.
27. Bachliński R, Duszyńska A, Kowalczuk A, Szmajke A, Łozak A. Zastosowanie metody GC-MS do charakterystyki *Calea zacatechichi* i *Psychotria viridis* – roślin kontrolowanych ustawą o przeciwdziałaniu narkomanii. *Problemy Kryminalistyki* 2013; 279(1):15-21.
28. Rodrigues E, Carlini EA. Plants with possible psychoactive effects used by the Krahô Indians, Brazil. *Rev Bras Psiquiatr* 2006; 28(4):277-282.
29. Mayagoita L, Diaz JL, Contreas CM. Psychopharmacologic analysis of an alleged onirogenic plant: *Calea zacatechichi*. *J Ethnopharmacol* 1986; 18(3): 229-243.
30. Cox G, Rampes H. Adverse effects of khat: a review. *Adv Psych Treat* 2003; 9:456-463.
31. Pantelis C, Hindler CG, Taylor JC. Use and abuse of khat (*Catha edulis*): a review of the distribution, pharmacology, side effects and a description of psychosis attributed to khat chewing. *Psychol Med* 1989; 19(3):657-668.
32. Al-Habori M. The potential adverse effects of habitual use of *Catha edulis* (khat). *Exp Opin Drug Saf* 2005; 4(6):1129-1138.
33. De Felice LJ, Glennon RA, Negus S. Synthetic cathinones: Chemical phylogeny, physiology and neuropharmacology. *Life Sci* 2014; 97:20-26.
34. Wabe NT, Mohammed MA. What science says about khat (*Catha edulis* Forsk)? Overview of chemistry, toxicology and pharmacology. *J Exp Integr Med* 2012; 2(1):29-37.
35. Basker GV. A review on hazards of Khat chewing. *Int J Pharm Pharmaceut Sci* 2013; 5(3):74-77.
36. Lumbreras EL, Ferrer-Gallego PP, Deltoro V, Ferrando I, Ortis DG. *Echinopsis pachanoi* (Britton & Rose) H. Friedrich & G D. Rowley (*Cactaceae*) primera cita como aloctona en España. *Bouteloua* 2013; 16:34-35.
37. Kvist LP, Moraes M. Plantas psicoactivas. In: Moraes MR, Øllgaard B, Kvist LP, Borchsenius F, Balslev H. (eds.) *Botánica Económica de los Andes Centrales*, Universidad Mayor de San Andrés, La Paz, 2006: 294-312.
38. Halberstadt AL, Geyer MA. Serotonergic hallucinogens as translational models relevant to schizophrenia. *Int J Neuropsychopharmacol* 2013; 16(10):2165-2180.
39. Crosby DM, McLaughlin JL. Cactus Alkaloids. XIX. Crystallization of mescaline HC1 and 3-methoxytyramine HC1 from *Trichocereus pachanoi*. *Lloydia* 1973; 36(4):416-418.
40. O'Mahony CS. *Psychoactive substances manual* (ed. 1.1). South Tipparary, UK: Health Service Executive 2010.
41. Bienvenu E, Amabeoku GJ, Eagles PK, Scott G, Springfield EP. Anticonvulsant activity of aqueous extract of *Leonotis leonurus*. *Phytomedicine* 2002; 9:217–223.
42. Oyedemi SO, Yakubu MT, Afolayan AJ. Antidiabetic activities of aqueous leaves extract of *Leonotis leonurus* in streptozotocin induced diabetic rats. *J Med Plants Res* 2011; 5(1):119-125.
43. Wua H, Lia J, Fronczeke R, Ferreira D. Labdane diterpenoids from *Leonotis leonurus*. *Phytochem* 2013; 91:229-235.
44. Jimoh FO, Adedapo AA, Afolayan AJ. Comparison of the nutritional value and biological activities of the acetone, methanol and water extracts of the leaves of *Solanum nigrum* and *Leonotis leonorus*. *Food Chem Toxicol* 2010; 48:964-971.
45. Jakubowska I, Choma J. Właściwości i oznaczanie substancji o działaniu psychoaktywnym. *Biuletyn WAT* 2013; 62 (2):123-143.
46. Popoola OK, Elbagory AM, Farouk A, Hussein A, Marrubiin. *Molecules* 2013; 18:9049-9060.
47. Souza RSO, Albuquerque UP, Monteiro JM, Amorim ELC. Jurema-Preta (*Mimosa tenuiflora* [Willd] Poir): a review of its traditional use, phytochemistry and pharmacology. *Braz Arch Biol Technol* 2008; 51:937-947

48. Silva VA, Gonçalves GF, Pereira MS, Gomes IF, Freitas AF, Diniz MF et al. Assessment of mutagenic, antimutagenic and genotoxicity effects of *Mimosa tenuiflora*. Brazil J Pharmacog 2013; 23(2):329-334.
49. Zippel J, Deters A, Hensel A. Arabinogalactans from *Mimosa tenuiflora* (Willd.) Poiret bark as active principles for wound-healing properties: specific enhancement of dermal fibroblast activity and minor influence on HaCaT keratinocytes. J Ethnopharmacol 2009; 124:391-396.
50. Pimentel LA, Correa FR, Gardner D, Panter KE, Dantas AF, Medeiros MRT et al. *Mimosa tenuiflora* as a cause of malformations in ruminants in the northeastern Brazilian semiarid rangelands. Vet Pathol 2007; 44(6):928-931.
51. Medeiros RM, de Figueiredo AP, Benício TM, Dantas FP, Riet-Correa F. Teratogenicity of *Mimosa tenuiflora* seeds to pregnant rats. Toxicon 2008; 51(2): 316-319.
52. Simonienko K, Waszkiewicz N, Szulc A. Roślinne środki odurzające – aktualnie obowiązująca lista w Polsce. Psychiatria Polska 2013; 47(3):499-510.
53. Nicasio Mdel P, Villarreal ML, Gillet F, Bensaddek L, Fliniaux MA. Variation in the accumulation levels of N,N-dimethyltryptamine in micropropagated trees and in *in vitro* cultures of *Mimosa tenuiflora*. Nat Prod Res 2005; 19(1):61-67.
54. Harizal SN, Mansor SM, Hasnan J, Tharakan JK, Abdullah J. Acute toxicity study of the standardized methanolic extract of *Mitragyna speciosa* Korth in rodent. J Ethnopharmacol 2010; 131(2):404-409.
55. Kumarsit E, Keawpradub N, Nuankaew W. Acute and long-term effects of alkaloid extract of *Mitragyna speciosa* on food and water intake and body weight in rats. Fitoterapia 2006; 77 (5): 339-345.
56. Compton DM, Garcia C, Kamaratos A, Johnson BG, Wedge T. An examination of the consequences of chronic exposure to *Mitragyna speciosa* during adolescence on learning and memory in adulthood. J Phytopharmacol 2014; 3(5):300-309.
57. Takayama H. Chemistry and pharmacology of analgesic indole alkaloids from the rubiaceae plant, *Mitragyna speciosa*. Chem Pharm Bull 2004; 52(8):916-928.
58. Karinen R, Fosen JT, Rogde S, Vindenes V. An accidental poisoning with mitragynine. Forensic Sci Int 2014; 245:e29-e32.
59. Agnihotri VK, ElSohly HN, Khan SI, Smillie TJ, Khan IA, Walker LA. Antioxidant constituents of *Nymphaea caerulea* flowers. Phytochemistry 2008; 69(10):2061-2066.
60. Emboden WA. Transcultural use of narcotic water lilies in ancient Egyptian and Maya drug ritual [Abstract]. J Ethnopharmacol 1981; 3(1):39-83.
61. Lavanya N, Senthil Kumar KL, Karthiyayini T. Pharmacognostical studies on seeds of *Nymphaea caerulea*. Res J Pharm Biol Chem Sci 2011; 2(2):28-35.
62. Kowalczyk A, Łozak A, Fijałek ZE. Aktywność biologiczna surowców roślinnych objętych Ustawą o przeciwdziałaniu narkomanii. Przegląd Medyczny Uniwersytetu Rzeszowskiego i Narodowego Instytutu Leków w Warszawie 2012; 3:318-333.
63. Aslam N, Wani AA, Nawchoo IA, Bhat MA. Distribution and medicinal importance of *Peganum harmala*. A review. Int J Adv Res 2014; 2(2):751-755.
64. Moloudizargari M, Mikaili P, Aghajanshakeri S, Asghari MH, Shayegh J. Pharmacological and therapeutic effects of *Peganum harmala* and its main alkaloids. Pharmacogn Rev 2013; 7(14):199-212.
65. Hemmateenjad B, Abbaspour A, Maghami H, Miri R, Panjehshahin MR. Partial least squares-based multivariate spectral calibration method for simultaneous determination of beta-carboline derivatives in *Peganum harmala* seed extracts. Anal Chim Acta 2006; 575(2):290-299.
66. Mohamed AHS, AL-Jammali SMJ, Naki ZJ. Effect of repeated administration of *Peganum harmala* alcoholic extract on the liver and kidney in Albino mice: A histo-pathological study. J Sci Innov Res 2013; 2 (3):585-597.
67. Yuruktumen A, Karaduman S, Bengi F, Flower J. Syrian rue tea: a recipe for disaster. Clin Toxicol (Phila) 2008; 46(8):749-752.
68. Tabudravu JN, Jaspars M. Anticancer activities of constituents of kava (*Piper methysticum*). South Pacific J Natur Sci 2005; 23:26-29.
69. Shi Y, Dong JW, Zhao JH, Tang LN, Zhang JJ. Herbal insomnia medications that target GABAergic systems: a review of the psychopharmacological evidence. Curr Neuropharmacol 2014, 12(3):289-302.
70. Johnston E, Rogers H. Introduction. In: Johnston E, Rogers H (eds.) Hawaiian Awa: views of an ethnobotanical treasure. Hawaii. Association for Hawaiian Awa 2006:1-7.

71. Jackson MC. The active ingredients in 'Awa (Kava, *Piper methysticum*). In: Jonston E, Rogers H (eds.) Hawaiian Awa: views of an ethnobotanical treasure. Hawaii. Association for Hawaiian Awa 2006:16-18.
72. Ujváry I. Psychoactive natural products: overview of recent developments. *Ann Ist Super Sanita* 2014; 50(1):12-27.
73. Jussofie A, Schmiz A, Hiemke C. Kavapyrone enriched extract from *Piper methysticum* as modulator of the GABA binding site in different regions of rat brain. *Psychopharmacology* 1994; 116(4):469-474.
74. Nowak G. Surowce roślinne o działaniu przeciwlękowym i antydepresyjnym. *Herba Polonica* 2009; (55)1:84-97.
75. Riba J, Valle M, Urbano G, Yritia M, Morte A, Barbanoj MJ. Human pharmacology of ayahuasca: subjective and cardiovascular effects, monoamine metabolite excretion, and pharmacokinetics. *J Pharmacol Exp Ther* 2003; 306(1):73-83.
76. Osmond H. Ololiuqui: the ancient Aztec narcotic remarks on the effects of *Rivea corymbosa* (Ololiuqui). *J Ment Sci* 1955; 101 (424):526-537.
77. Piekoszewski W, Florek E. Dopalacze. *Przeegl Lek* 2009; 66(10):861-865.
78. Rech MA, Donahey E, Cappiello Dziedzic JM, Oh L, Greenhalgh E. New drugs of abuse. *Pharmacotherapy* 2015; 35(2):189-197.
79. Cunningham CW, Rothman RB, Prisinzano TE. Neuropharmacology of the naturally occurring κ -opioid hallucinogen salvinorin A. *Pharmacol Rev* 2011; 63(2):316-347.
80. Orton E, Liu R. Salvinorin A. A mini review of physical and chemical properties affecting its translation from research to clinical applications in humans. *Transl Perioper Pain Med* 2014;1(1):9-11.
81. Antonio T, Childers SR, Rothman RB, Dersh CM, King C, Kuehne M et al. Effect of Iboga alkaloids on μ -opioid receptor-coupled G protein activation. *PLoS One* 2013; 8 (10): e77262. doi:10.1371/journal.pone.0077262.
82. Bulling S, Schicker K, Zhang YW, Steinkellner T, Stockner T, Gruber CW et al. The mechanistic basis for noncompetitive ibogaine inhibition of serotonin and dopamine transporters. *J Biol Chem* 2012; 287(22):18524-18534.

ROŚLINY PSYCHOAKTYWNE W DOPALACZACH JAKO ZAGROŻENIE DLA ZDROWIA PUBLICZNEGO

AGNIESZKA RONDZYSTY¹, KAROLINA DZIEKAN^{2*}, ALEKSANDRA KOWALSKA²

¹Zakład Nauk Humanistycznych w Medycynie
Pomorski Uniwersytet Medyczny
ul. Chłapowskiego 11
70-103 Szczecin

²Zakład Komórek Macierzystych i Medycyny Regeneracyjnej
Instytut Włókien Naturalnych i Roślin Zielarskich
ul. Kolejowa 2
62-064 Plewiska

*autor, do którego należy kierować korespondencję:
e-mail: karolina.dzieskan@iwnirz.pl

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 młodzieży, 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*