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REVIEW ARTICLE

# Drug-abuse poisoning: new substances in the 21st century

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Mind-altering substances have been used throughout history. The earliest psychoactive drugs were derived from plants, but technological advances have introduced substances that have been synthesized de novo or that result from modifications of older drugs. Millions now experiment with such substances or use them recreationally. Certain drugs have traditionally been linked to specific social or cultural groups: for example, we associated reggae with marijuana, young urban professionals (yuppies) with cocaine, and electronic music fans with amphetamines. Such ties are unsupported, however, from the health care professional's vantage, not only because the market for any type of drug is more widespread than any of these social settings but also because it is common for users to combine several substances in pursuit of different effects. Several drugs are sometimes used on a single night. Street drugs cause of a large number of medical problems that lead users to seek emergency care. This review discusses the most common new substances on the street at the beginning of the 21st century and their effects on health. [Emergencias 2014;26:472-480]

**Keywords:** Drug abuse. Emergency health services. Poisoning.

The use of mind-altering substances is probably almost as old as humanity itself. Their discovery was probably incidental on consuming certain plants or mushrooms containing psychoactive ingredients, but these substances began to be used for mystical, religious, ceremonial and even recreational purposes. Gradually the spectrum of substances broadened, until about 5,000-6,000 BC when a product derived from the fermentation of grapes (wine), with ethyl alcohol as its active ingredient, became the addictive substance most consumed by humans, associated in turn with a major economic activity in many societies and, in cases of abuse, the cause of many diseases. Probably no other poison has been more associated with human morbidity and mortality than ethanol, which continues today[1,2].

The late nineteenth century marked a milestone in the evolution of drugs, when a German chemist, Dreser, synthesized heroin (diacetylmorphine) in 1883. Initially it had a medical use, but later became a substance of abuse that marked the starting point of a plague of addiction to opiates which peaked in the 1980s and is currently in decline[3,4].

A world apart is that of cocaine, a mildly addictive substance in its natural state, as the active principle of Erythroxylum coca, but manipulated in clandestine laboratories has led to a series of derivatives (cocaine hydrochloride, crack and basuko among others), a very powerful psychostimulant, more addictive than the natural compound, which has spawned a host of consumers and cases requiring urgent medical attention[5-9], some of them related to its illegal transport[10-14].

The pharmaceutical industry, many of whose products have helped improve human health, has also made available other drugs that are used with non-curative intent, many of them addictive, while many individuals have engaged in clandestine synthesis of chemicals, for the sole purpose of finding consumers eager to experiment with substances that alter mood and sensory perceptions, called synthetic drugs[15].

According to official data, about 85 million American adults (one in four) have used an illegal drug at some point in their lives. Cannabis is the

most commonly used (77 million), but the rates of consumption of other drugs are also very high (14.5 million cocaine users, 12.7 million amphetamine users and 11.4 million ecstasy users) 2. If we consider specific populations (Eg. UK disco customer surveys), the prevalence of substance use is much higher since, for example, 40% of respondents reported having used ketamine in the past year and 2% GHB (gamma-hydroxybutyrate)[16].

It is difficult to accurately estimate the total number of drug users requiring emergency assistance. The Spanish Drugs Observatory (OED) publishes an indicator called "hospital emergency department attention of psychoactive substance users" which since 1987 has monitored the evolution and characteristics of drug use, but the method of data collection does not reveal the precise numbers of patients seen[17]. However, some studies have allowed quantifying ED visits related to recreational drug abuse, accounting for 2-3% of total ED visits in a tertiary hospital[18]. The present work reviews emerging drug abuse leading to ED visits in the early twenty-first century. For space reasons, this review excludes opiates, cocaine and ethyl alcohol, a frequent cause of ED visits, where emergency physicians and toxicologists have together contributed to defining the clinical features of the most frequent adverse effects[19-21].

## Cannabis and synthetic cannabinoids (SPICE)

Cannabis id derived from the plant Cannabis sativa, with several subspecies: ruderalis, mainly cultivated for its fibers and oil; sativa, poor in active ingredients; and indica, which contains a higher concentration of cannabinoids and more than 70 different compounds, which differ depending on the variety, origin or climate. The main psychoactive principal is δ-9-tetrahydrocannabinol ($\Delta^9$-THC) and its concentration determines the potency of cannabis derivatives.

In the mid-first decade of this century, there appeared on the synthetic drug market certain mixtures of "natural" substances with synthetic cannabinoids, called Spice. With similar effects to cannabis and sold on the online market, it was a legal alternative to marijuana, labeled as incense or products unfit for human consumption. Its composition is difficult to determine. Various natural psychotropic substances and synthetic cannabinoids have been identified (dibenzopirans, aminoalkilindols and ciclohexilfenols) with much higher affinity for the CB1 receptor than THC[22]. All these products have been introduced onto the market without having been subjected to clinical or toxicological studies.

The acute effects of natural cannabis are highly variable, depending on the personality and consumer experience, expectations or concentration of $\Delta^9$-THC. A joint (usually tobacco and cannabis leaves rolled into a cigarette) typically contains between 5 and 30 mg of $\Delta^9$-THC, of which 0.5 to 7.5 mg is absorbed, when the dose needed to produce effects in humans is from 2 to 22 mg. Symptoms sought by the consumer are euphoria, wellbeing, relaxation, drowsiness, impaired time perception and increased appetite, but are highly variable depending on the dose adsorbed (Table 1). Cannabis use is associated with an increased risk of cardiovascular disease, neurovascular disease or PAD[8,23]. Chronic cannabis use in regular amounts initiated at early ages (teens) has been associated with cognitive impairment, learning deficits and brain volume changes[24].

The most common reasons for visiting the emergency department are anxiety, panic attacks and acute psychosis. The physician must always consider all other drug use, as many hallucinogenic drugs at low doses may produce similar clinical effects.

Synthetic cannabinoids produce a similar clinical picture to that of cannabis, with conjunctival redness, tachycardia, dry mouth and alterations of mood and perception, but of much greater inten-

**Table 1.** Effects of cannabis, according to amount of THC absorbed.

| Dose | THC absorbed | CNS manifestations |
|---|---|---|
| Low | 0.5-7.5 mg | Euphoria, easy laughter, hilarity, altered perception of time, changes in the perception of colors or sounds. Wellbeing, relaxation, drowsiness, poor concentration and memory. Conjunctival hyperemia, mydriasis, abolition of light reflex. Oral and mucosal dryness, increased appetite. |
| High | ≥ 15 mg | Marked distortion in temporal, visual and auditory perception. Hallucinations, anxiety, paranoia, feelings of depersonalization and unreality, confused and disorganized thoughts. Tachycardia, palpitations |
| Very high | > 20-25 mg | Panic attacks, toxic delirium (confusion, memory disturbances, suspiciousness, depersonalization, unreality, fear and sensory perception disorders), paranoid psychosis, depression. Altered consciousness may appear, and can reach deep coma. Can also cause arterial hypertension and angina. Cases of ischemic stroke have also been described. |

THC: tetrahydrocannabinol; CNS: central nervous system.

sity and duration (mean duration 6 hours). They have also been associated with cerebral ischemic events[25]. Consuming large amounts may cause functional psychosis of rapid onset, with restlessness, aggressiveness and a mix of affective symptoms – maniac and hypomanic – and psychotic symptoms, which can last for as long as 6 weeks. Furthermore, the lack of scientific studies on its effects (many of these substances are experimental) means their consumption entails a risk of serious and unpredictable health problems.

Synthetic cannabinoids are typically undetectable with hospital analytical techniques, as they have a different chemical structure to THC and the immunoenzymatic technique used to detect their presence in urine gives negative results.

Treatment of acute poisoning is symptomatic, since there is no antidote for THC. The patient should be in a relaxed atmosphere and, if drugs are needed, benzodiazepines are used. If psychotic symptoms predominate, olanzapine is recommended. If the route of administration of cannabis is ingestion (accidents in children, body-packers) and the patient is attended within two hours of ingestion, decontamination with activated charcoal is indicated.

## MDMA and amphetamine derivatives

MDMA (3, 4-methylenedioxymethamphetamine) or ecstasy is a derivative of the amphetamine molecule (hence the recent slang term Molly). It is sold in tablet form (50-150 mg) or crystalline powder in capsules, and in Spain is called crystal or just M. The composition includes contaminants (caffeine, lidocaine, paracetamol, mcpp, cocaine, diazepam, ketamine and others) that may enhance the effects or cause symptoms not related to MDMA (Figure 1)[26]. Occasionally, tablets supposedly containing MDMA have been shown to actually contain methamphetamine[27].

The main effects sought by the consumer of ecstasy are euphoria, vigor, increased libido, increased sensory perception (mainly visual), extraversion, feeling good and closeness with others. It may be accompanied by hyperthermia due to the direct effect on the thermoregulatory center in the central nervous system (CNS). Stereoisomers (or S + R) of MDMA confer different capacities, so sympathomimetic effects may predominate (S +) or hallucinations (R-).

The mechanism of the most serious complications of MDMA depends on 3 main factors: muscle activity, the direct effect on serotonin and catecholamines, and increased vasopressin (Figure 2). Symptoms that occur most frequently are summarized in Table 2.

**Figure 1.** Different pills of amphetamine derivatives, contributed by patients seen in the emergency department.

The diagnosis is clinical. There must be suspicion of poisoning by MDMA or other amphetamine derivatives in patients with hyperthermia, hypertension and tachycardia, associated with altered mental status and muscle tone (hypertonia). Consumption is confirmed by the presence of amphetamine metabolites in urine. It is advisable to test for electrolytes, cardiac enzymes, serum creatinine, CK, myoglobinuria, transaminases and coagulation[28] to rule out other complications such as renal failure and rhabdomyolysis.

Treatment is aimed at controlling the symptoms, since there is no antidote for amphetamines. Benzodiazepines are the drug of choice for anxiety symptoms and those associated with sympathetic hyperactivity.

But MDMA, MDA (3,4-methylenedioxymethamphetamine) and MDEA (3,4-methylenedioxy-N ethylamphentamina) are just the tip of the iceberg of a large amount of amphetamine derivatives that have been introduced over the last 30 years as synthetic drugs, as is the case of 4-bromo- 2,5-dimethoxyamphetamine (DOB), 4-bromo-2,5-methoxyphenylethylamine (2CB), 4-methyl-2,5-dimethoxyamphetamine (DOM) or paramethoxyamphetamine (PMA) among over 200 compounds[29], although the prevalence and frequency of consumption of these substances are still low compared to the classic amphetamine derivatives.

## Liquid ecstasy (GHB)

Gamma-hydroxybutyrate (GHB) or liquid ecstasy is a CNS depressant derived from γ-aminobutyric acid (GABA), with euphoric effects similar to those of ethyl alcohol and used as a recreational substance since the end of the last century[30]. Today it has become a common substance on the

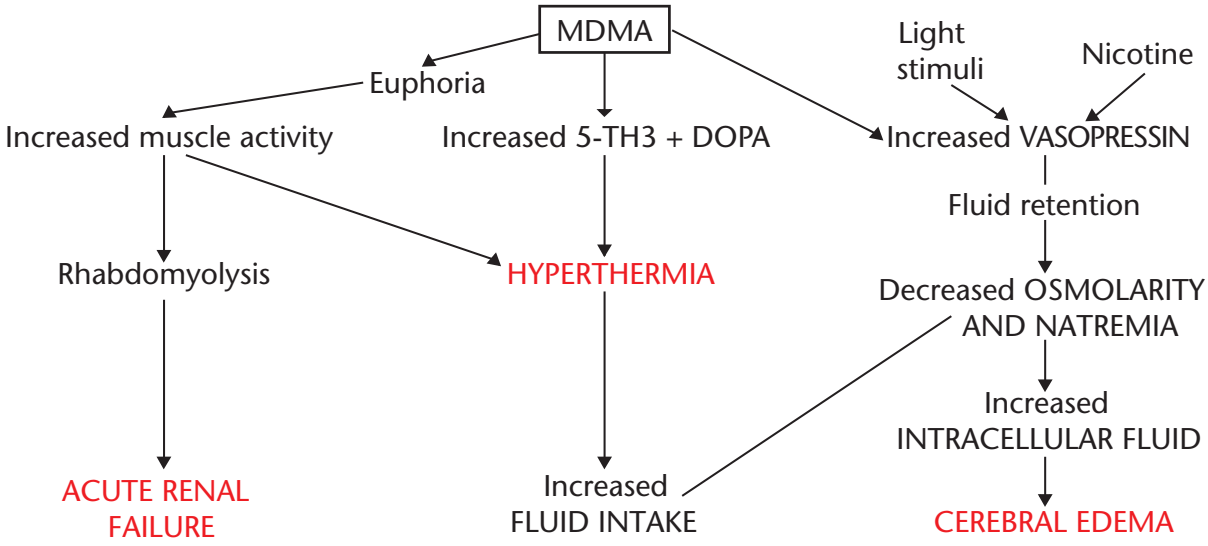


**Figure 2.** Pathophysiology of overdose of MDMA (metilenodioximetanfantamina).

market for recreational drugs and, sometimes, it has also been used to facilitate criminal robbery and rape (chemical submission)[31].

GHB is often presented in ampoules of 10 mL (Figure 3) and is consumed orally, mixed with beverages or drugs such as cocaine, cannabis, amphetamines and hallucinogens. Its effects are enhanced by other CNS depressants, so severe poisoning can occur with low doses of GHB[32]. Looking consumed their disinhibitory, aphrodisiac and euphoric effects or involuntarily administers to victims of chemical submission by their ability to produce amnesia.

GHB overdose presents a clinical picture characterized by a decreased level of consciousness, sometimes reaching the level of coma, which can be of rapid onset, deep, hypotonic and hyporeflexive. Usually the coma is of very short duration followed by spontaneous recovery[33]. Some cases develop respiratory arrest. In the recovery phase, the patient may have fluctuations of awareness, show uninhibited behavior and retrograde amnesia, and symptoms which vary depending on the dose, personal tolerance and other substances concomitantly consumed (Tables 3 and 4).

GHB can only be detected in blood or urine using gas chromatography and mass spectrometry but not by routine toxicological analysis, so its presence is usually unconfirmed in clinical practice. Moreover, its half-life is very short and the chances of detection decrease significantly after 8 hours of consumption. The clinical diagnosis is based on history of the patient or companions. Fluctuating level of consciousness is typical, including coma followed by rapid recovery.

Treatment of acute poisoning is symptomatic, especially respiratory support when necessary. There is no antidote and although some drugs

**Table 2.** Clinical manifestations of overdose of MDMA

| | |
|---|---|
| Cardiovascular symptoms | Palpitations, arrhythmias, angina. |
| Neurological symptoms | Headache, aphasia, ataxia, muscular hypertonia, seizures, coma. |
| Psychiatric symptoms | Agitation, anxiety, racing thoughts, paranoia, panic, delirium, insomnia, psychosis. |
| Other symptoms | Hyperemesis, rhabdomyolysis, renal failure, hyperthermia (heat stroke), bruxism, toxic hepatitis. |
| Residual symptoms (up to 48 h after intake) | Depression, fatigue, lack of concentration. |

MDMA: metilenodiocimetanfantamina.

**Figure 3.** Different presentations of gamma-hydroxybutyrate (GHB) found among the belongings of patients seen in the emergency department for overdose.

have been used empirically (naloxone, flumazenil or physostigmine), none has proven efficacy[34]. Digestive decontamination or renal extraction are not indicated.

Continued use of GHB is associated with a risk of addiction that involves repeated self-administration, development of tolerance and craving or compulsive search. In addicts, a withdrawal syndrome has been described, with tremor, insomnia, anorexia, nausea, hypertension, tachycardia, anxiety, sweating, agitation, delirium and convulsions, which may occur after continued consumption of 2 or 3 months, but depends on usual dose and the interval between consumption episodes[35]. Wernicke-Korsakoff syndrome induced by GHB has been reported[36].

The diagnosis of GHB withdrawal syndrome is by exclusion. It must be suspected in habitual consumers who, about 3-6 hours after the last dose, present with severe shaking or trembling, and whose medical records report previous multiple GHB poisoning or episodes of loss of consciousness or seizures, with complete recovery at discharge.

Lately the abuse of GHB precursors such as 1, 4-B (1, 4-butanediol) and GBL (gamma butyrolactone) has been detected; these are chemicals for industrial use as solvents and derivatives for human consumption, since after oral intake they are rapidly metabolized to GHB[37-39].

## Ketamine

Ketamine is a dissociative general anesthetic, with effects on the level of consciousness and the unconscious. It causes intense psychic sensations and illusory states during anesthesia and awakening, which has lead to lowered clinical use and it has become, at the same time, a recreational substance of abuse. In commercial form it is used unlawfully IV or IM, or dried in the oven, microwave or over low heat, turning it into powder which is consumed orally, smoked or snorted. Ketamine combines hypnotic, analgesic and amnesic effects without loss of consciousness or respiratory depression. Some consumers use it to reduce the negative side effects of cocaine or amphetamines (jaw tension); others seek its hallucinogenic and depersonalization effects[40].

Ketamine users report a dissociated state, as if out of the body, with a sensation of floating, accompanied by hallucinations and difficulty moving, usually starting with anxiety, and paresthesia. Subsequently there is loss of body control and paralysis. At higher doses, it causes impaired time perception, depersonalization (feeling of being unreal) derealization (feelings that the environment is unreal), extracorporeal perceptions (out of the body) and near-death experiences (Table 5).

Ketamine is not detected in routine analysis for drugs of abuse based on enzyme immunoassay techniques, so the consumption or overdoses of ketamine are probably underdiagnosed. The identification of this drug requires a technique based on gas chromatography, and it can be detected up to 72 hours after a single dose or more in chronic users.

**Table 3.** Effects of gamma-hydroxybutyrate (GHB) according to dose consumed.

| | |
|---|---|
| Low doses (0.5-1.5 g) | Relaxation, increased sociability, decreased motor skills, dizziness, increased 3-D perception. |
| Medium doses (1.5-2.5 g) | Increased musical perception, dizziness, difficulty to accommodate visual focus, mood swings, nausea, pro-sexual effects (increased sense of touch and the desire to touch, increased libido and sensuality, with greater erection capacity and more intense orgasms), drowsiness, disorientation, altered behavior. |
| High doses (> 3 g) | Vomiting, seizures, delirium, coma. |

**Table 4.** The most common clinical manifestations of GHB poisoning *

| | |
|---|---|
| Central nervous system | |
| Nonspecific neurological symptoms (headache, feeling of instability, convulsions, disorientation, impaired language) | 60% |
| Behavioral changes (aggression, disinhibition, emotional lability) | 22% |
| Altered consciousness according to GCS: | |
| – GCS 3-8 | 50% |
| – GCS 9-12 | 23% |
| – GCS 13-15 | 27% |
| Pupils | |
| – Mydriasis | 42% |
| – Miosis | 26% |
| – Means | 32% |
| Respiratory apparatus | |
| Signs or symptoms (cough, dyspnea) | 17% |
| Bradypnea (BR <10 breaths / min) | 14% |
| Hypoxemia (SaO2 <95%) | 11% |
| Cardiovascular system | |
| Various symptoms (palpitations, chest discomfort not suggestive of ischemic heart disease) | 15% |
| Bradycardia (HR <60 beats / min) | 17% |
| Hypotension (SBP <90 mmHg) | 3% |
| Digestive apparatus | |
| Various symptoms (nausea, vomiting, abdominal pain) | 28% |
| Other manifestations | |
| Hypothermia (Temp <35.5) | 11% |

*Data from a series of 464 cases of GHB poisoning collected in the emergency room of the Hospital Clínic of Barcelona. Patients sometimes had combined manifestations. GCS: Glasgow Coma Scare; GHB: gamma-hydroxybutyrate; BR: breathing rate; SatO2: oxygen saturation; HR, heart rate; SBP, systolic blood pressure.

Ketamine has no antidote, so the therapeutic measures to be applied are generally symptomatic and support. Certain drugs (agonists alpha-2-adrenergic as doxapram) have been proposed as antidotes of ketamine, but in cases of respiratory depression the best choice is mechanical ventilation.

Coma patients wake up in a few hours, although sedation may persist for 24 hours. If there is anxiety or hallucinations, benzodiazepines can be used while psychotic behavior may require the use of neuroleptics like haloperidol.

Continued use of ketamine results in tolerance and decreased intensity and duration of the psychedelic experience, which may even disappear completely. It is associated with a variety of psychiatric problems (persistent hallucinations, personality fragmentation, mania, depression, suicidal thoughts) and sleep disorders (insomnia, nightmares, night terrors). It can cause high psychological dependence and impaired memory and learning, and chronic users have described the occurrence of bladder dysfunction and interstitial cystitis[41]. Flashbacks similar to those sometimes experienced with LSD, i.e. episodes lasting seconds in which, without ketamine consumption, the subject experiences changes in perception, somatic symptoms and amnesia; similar but not exact repetition of previous experience has also been reported[42]. The effects of chronic use may take months or even years to disappear after quitting.

Recently (2010) a derivative of ketamine, methoxemethamine, with theoretically less effects on the bladder and less toxicity has appeared on the market. However, symptoms of acute cerebellar toxicity and serious sympathomimetic pictures have been associated with its use[40,43].

**Table 5.** Clinical manifestations of overdose of ketamine.

| | |
|---|---|
| Cardiovascular symptoms | Palpitations, tachycardia, hypertension, angina, cardiac arrest. |
| Neurological symptoms | Headache, dizziness, vertigo, ataxia, dysarthria, tremor, dystonia, seizures, neuropathy, amnesia, increased ICP, coma, tinnitus, paresthesia, paralysis, seizures. |
| Respiratory symptoms | Bradypnea, pneumonia, respiratory arrest. |
| Ocular symptoms | Diplopia, nystagmus, mydriasis, blurred vision, increased IOP. |
| Psychiatric symptoms | Anxiety, disorientation, agitation, delirium, hallucinations, panic attacks, loss of control and body awareness, altered time perception, OBE's, NDE's, psychosis, paranoia, suicidal ideas. |
| Trauma symptoms | Analgesia may mask any type of injury sustained. |
| Digestive symptoms | Nausea, vomiting, abdominal pain. |

PIC: intracranial pressure; IOP: intraocular pressure; OBE's: out of body experiences (vision of the body while the mind is floating in space); NDE: near death experiences.

## Poppers

Poppers are a series of volatile substances (amyl nitrite, butyl nitrite, isobutyl nitrite, cyclohexyl nitrite, ethyl nitrite), which theoretically are for recreational use due to their aphrodisiac, sphincter relaxing, delayed ejaculation and orgasm intensifying effect. They are presented in 10-15 mL plastic bottles and are readily available in sex shops or online stores (Figure 4). Inhaled, or less frequently ingested, they are irritating to mucous membranes and may cause burns. Normally their ingestion is accidental or involves novice users.

Nitrites are highly soluble substances. They are rapidly absorbed and readily cross the blood brain barrier. The effects last about 20-40 min. Nitrates cause smooth muscle relaxation. Their toxicity is due to oxidant activity to convert ferrous iron ($Fe^{+2}$) of hemoglobin in ferric iron ($Fe^{+3}$), leading to methemoglobin (MHb). This process prevents hemoglobin from transporting oxygen to tissues properly, so multiple organ tissue hypoxia is possible with normal $pO_2$[44]. The tell-tale sign of popper use is cyanosis without hypoxemia. The severity of symptoms is directly related to the concentration of methemoglobin (MHb), which also determines the treatment (Table 6).

Popper use can also lead to hemolytic anemia which may be acute or detected after 24-48 hours, and even much later, so that all these patients must be followed as outpatients.

The diagnosis of popper poisoning is clinical and can be confirmed by non-invasive pulse oximetry or by measuring the concentration of MHb in a sample of arterial or venous blood. In the anamnesis it is especially important to establish the dose and time since consumption.

The effects of MHb are reversed with methylene blue[45]. The aim is to decrease MHb to less than 10%. When contraindicated (very young children or patients with a deficit of 1.6 glucose phosphate dehydrogenase), ascorbic acid (vitamin C) can be used, 1 g IV every hour, up to 10 g. In very serious cases (MHb > 40-60%), insufficient response or contraindication to methylene blue), exchange transfusion is indicated.

## Energy drinks

These comprise a number of products of very


**Figure 4.** Preparation of poppers, contributed by a patient treated in our hospital.

variable composition (water, sugar, caffeine, vitamins, herbs, amino acids, proteins) that are available in bars, supermarkets and service stations, and consumed as beverages. About 30% of adults aged 18 to 65 years and 68% of adolescents between 10 and 18 take these drinks regularly, according to the European Food Safety Authority[46].

As possible substances of abuse, the most dangerous ingredient composition is caffeine, but they usually also contain other substances such such as taurine, which increases cardiac contractility, or inositol, which enhances the effects of caffeine and taurine[47].

Caffeine is a stimulant alkaloid; excessive consumption can cause tachycardia, cardiac arrhythmias, palpitations, insomnia, dystonia, tremor, polyuria. A cup of espresso contains about 80-100 mg of caffeine. The amount of caffeine in each energy drink varies between 30 and 35 mg / 100 ml. There is a clear relationship between dose and symptoms, so that intakes above 750 mg can cause metabolic acidosis and hypotension and a dose of 5 g may be fatal.

The consumption of alcohol and energy drinks represents an added risk factor. The stimulant effects of caffeine can camouflage the sedative effects of alcohol, promote an increase in the total dose of alcohol consumed and the result is a high rate of alcohol in blood without any perception of risk[48].

There is no specific treatment or antidote for overdoses of such substances. Benzodiazepines are the drug of choice for symptomatic control of arrhythmias, anxiety, or tremors. If coexisting alcohol poisoning or more serious situations (hypotension, metabolic acidosis), general supportive measures should be provided.

## Research chemicals

So-called research chemicals (RC) are a series of chemicals with preferential effects on the CNS; their action is very similar to those of amphetamine or cocaine, and in recent years RC have joined the catalog of substances used for recreation[49]. They are also called legal highs or new synthetic substances, although some of them were synthesized over 30 years ago and others are just old drugs that are used for different purposes for which they were synthesized[50].

They come from many chemical families, although the main group is derivatives of tryptamines and phenethylamines. They can be easily obtained online, usually labeled as agricultural products, bath salts or plant fertilizers, providing them with a pseudo-legal status which allows their sale[51]. These products have scarcely been subjected to clinical research in humans and the great amount of internet information is unreliable (most of the available information comes from first-person accounts of users in forums or chats on the internet)[52].

RC can be classified according to their chemical origin (tryptamines, phenethylamines, piperazines, arilciclohexilaminas, piperidines, local anesthetics or synthetic cannabinoids) or according to

**Table 6.** Approximate correlation between the concentration of methemoglobin (MHb) and clinical manifestations, and treatment proposed[35]

| MHb (%) * | Clinical Manifestations | Treatment |
|---|---|---|
| < 2% | None | None |
| 2-9% | None or cyanosis | 100% oxygen mask |
| 10-19% | Cyanosis | 100% oxygen mask + 1 mg / kg of methylene blue |
| 20-39% | Nausea and vomiting, cyanosis, neurological symptoms and metabolic acidosis ** | 100% oxygen mask + 1.2 mg / kg of methylene blue |
| 40-59% | Marked cyanosis, neurological symptoms, metabolic acidosis and symptoms | 100% oxygen mask + 2.4 mg / kg of methylene blue<br>Consider transfusion according to clinical condition |
| > 60% | Intense cyanosis, neurological symptoms, very intense metabolic acidosis and risk of cardiac arrest | 100% oxygen mask + 4.6 mg / kg of methylene blue<br>Exchange transfusion |

* Patients with underlying pathology (hematologic, respiratory or cardiac) may have more severe symptoms with lower concentrations of MHb
** Neurological symptoms: instability, headache, anxiety, blurred vision, restlessness, stupor, weakness, coma, convulsions. ***Cardiocirculatory symptoms: dyspnea, tachypnea, tachycardia, syncope, arrhythmias, hypotension, shock.

their effects on the CNS (stimulants, depressants, hallucinogens, antipsychotics). Many substances can have different effects depending on whether they are consumed jointly with other substances, or even consumer susceptibility and time of consumption. Given their large number (mephedrone, methylone and many others), this review cannot describe the effects of each one. Generally, they have sympathomimetic symptoms (tachycardia, hypertension, tremor, anxiety) and, theoretically, specific effects (hallucinogenic, entactogenic, aphrodisiac) of each drug. These substances have not been tested in humans before being marketed, so that the effects of their sporadic or chronic consumption are not predictable, as opposed to traditional drugs.

In cases of overdose, there are no specific antidotes. In general, treatment is aimed at establishing hemodynamic, metabolic and respiratory support in the most relaxing environment possible, and symptom control. Benzodiazepines are used to treat sympathomimetic symptoms and neuroleptics for agitation or delirium. Digestive tract decontamination measures are not indicated.

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## Intoxicaciones por drogas de abuso: sustancias emergentes en el siglo XXI

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Mind-altering substances have been used throughout history. The earliest psychoactive drugs were derived from plants, but technological advances have introduced substances that have been synthesized de novo or that result from modifications of older drugs. Millions now experiment with such substances or use them recreationally. Certain drugs have traditionally been linked to specific social or cultural groups: for example, we associated reggae with marijuana, young urban professionals (yuppies) with cocaine, and electronic music fans with amphetamines. Such ties are unsupported, however, from the health care professional's vantage, not only because the market for any type of drug is more widespread than any of these social settings but also because it is common for users to combine several substances in pursuit of different effects. Several drugs are sometimes used on a single night. Street drugs cause of a large number of medical problems that lead users to seek emergency care. This review discusses the most common new substances on the street at the beginning of the 21st century and their effects on health. [Emergencias 2014;26:472-480]

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