UCL School of Pharmacy

Hegal Drugs Abuse 2025

Illegal drugs of abuse

A broad range of psychoactive substances that are illegal to possess/distribute, taken for short-term pleasurable effects – long-term use may lead to **dependency**, **tolerance** and possible **withdrawal symptoms** on abruptly stopping the drug.



Illegal drugs of abuse

Drugs with abuse potential all produce a common rewarding effect – involving increased activity of **dopaminergic neurones** in the **mesolimbic dopaminergic pathway** of the brain running from the VTA to nucleus accumbens and other *limbic* regions.



Mesolimbic dopaminergic reward circuit



Illegal drugs of abuse

The same mesolimbic release of **dopamine** and production of pleasure sensations can be produced by other drugs of abuse *e.g.* **morphine**, **heroin**, **cocaine**, **amphetamine**, **ecstasy**, **cannabis**, and also **alcohol** and **nicotine**, hence their common potential for abuse.



Other neuronal pathways in addiction



Hipp, hippocampus; Thal, thalamus; VP, ventral pallidum; PFC, prefrontal cortex; NAcc, nucleus accumbens; VTA, ventral tegmental area; BLA, basolateral amygdala.

Heroin and related



What are opiates?

• Opiates (morphine, codeine) are extracted from opium, the dried latex ('milk') harvested from the seed-pod of the Asian poppy, *Papaver somniferum*.



 Opiates are classed as narcotic analgesics used to relieve pain with no loss of consciousness – but they have a high potential for abuse – they bind to μ, δ, and κ opiate receptors in the CNS.

The opium poppy



Papaver somniferum

The opium poppy



Afghanistan produces more than 90% of illicit heroin globally, and more than 95% of the European supply (2021). This is despite the \$8.4 billion apparently spent by the US in counternarcotics programs.

Opium alkaloids





Morphine

Codeine

What are opiates?

• Other opiate-related synthetic drugs:

Heroin, methadone, buprenorphine, dihydrocodeine, pethidine, fentanyl, remifentanil, dipipanone, oxycodone, hydrocodone, hydromorphone, meptazinol, tramadol, dextromethorphan, pentazocine, tapentadol.

• **Opiates:** are used medically to relieve severe pain without causing loss of consciousness, but also have a high potential for abuse.





Heroin (diacetylmorphine)



Heroin is a highly addictive synthetic opiate derived from the opium resin

Heroin

• Heroin (diacetylmorphine) – first synthesized from morphine in 1874 - introduced in medicine in 1898 as a safe, non-addictive remedy for morphine addiction !! Later, was sold as a specific treatment for coughs.

• Heroin produced dependency very rapidly in some individuals.

• Heroin and other opiates - made illegal in UK in 1920 with arrival of Dangerous Drugs Act.



Heroin

• Pure heroin: white odourless, crystalline powder with a bitter taste. Most illicit heroin varies in colour from white to dark brown powder (due to impurities or additives), which is dissolved in water and injected. Street heroin may cost ~£10 a bag (100 mg).

 Most street-bought preparations of heroin are diluted ('cut') with glucose, starch, baking soda, powdered milk, or other substances such as caffeine, quinine, flour, chalk and talcum powder. The amount of actual heroin in a cut batch can then range from ~3-99%. There is no way to know the purity of a batch.

How is heroin administered?

Street users usually inject opiate solutions under the skin **("skin popping")** or directly into a vein or muscle.

The drugs may also be "snorted" into the nose, smoked (where high purity heroin is available), or taken orally or

rectally.



Injection - most practical way to administer low-purity heroin -snorting may be preferred by new users as it eliminates risk of acquiring syringe-borne diseases:-HIV/AIDS, hepatitis, and stigma of i/v heroin use.

What are the effects of heroin?

- Short-term effects of injected heroin appear in ~7-8 seconds -disappear in a few hours or days. Heroin rapidly enters brain -converted to morphine- binds to opioid receptors (μ , δ , κ). Heroin makes user feel intense pleasure ("high").
- When smoked or sniffed, peak effects are less intense- usually felt in ~10-15 minutes.

• After initial CNS stim; higher brain centres are depressed: \downarrow coughing and breathing reflexes; \downarrow heart rate; extremities feel heavy; mouth is dry.

What are the effects of heroin?

 Side-effects: restlessness, nausea, vomiting, shallow breathing, constipation, itching, cold skin, sleepiness.
Pupils constricted (miosis).

 After very large doses, user cannot be awakened; pinpoint pupils, skin cold, moist, bluish; profound respiratory depression → coma and death.

• Overdose and death are common, particularly on the street, where the amount of drug contained in a "hit" cannot be accurately gauged.





Opiate receptor coupling



PI3K: Phosphatidylinositol 3-kinase

Effects of long-term heroin use

Long-term complications appear after repeated opiate use over a long period.

 Injecting heroin regularly can lead to scarred and/or collapsed veins. Chronic opiate users may develop *endocarditis,* due to unsterile injection techniques.

• Smoking heroin regularly can lead to *pneumonia* and other lung complications. Loss of appetite can result in malnutrition. Chronic constipation is also common. Women can have irregular periods and men can become impotent.

Effects of long-term heroin use

• Serious personal problems can develop. Using drugs can become more important than family and friends.

 Babies born to heroin-addicted mothers are often premature and underweight, and go through withdrawal at birth (Neonatal Abstinence Syndrome; :NAS) They can be infected with HIV, hepatitis or blood poisoning.



• Drug users who share needles are at a high risk of acquiring HIV infection and developing AIDS.





Effects of long-term heroin use

• Unsterile injection techniques can also cause skin abscesses, cellulitis, hepatitis B and C), and even brain damage. Tetanus is also common.

• **Repeated sniffing of heroin** damages the nose.





Tolerance and dependence

Tolerance: with regular long-term use (or even occasional use over a long period of time) - needing more and more of drug to get the same intensity of effect, develops tolerance to many of the desired effects of the opioids.

Chronic users may also become psychologically and physically dependent on opioids, due to neurochemical and molecular changes in the brain.



Tolerance and dependence

Psychological dependence: exists when a drug is so central to a person's thoughts, emotions, and activities that the need to continue its use becomes a craving or compulsion.

With physical dependence: body has adapted to presence of drug, and withdrawal symptoms of discomfort (similar to flu) occur if use of drug is reduced or stopped abruptly; positive pleasure is replaced by relief at simply taking the drug to maintain 'normality'.

Withdrawal symptoms

• Withdrawal from opioids may occur as early as a few hours after the last administration.

• Symptoms include:



restlessness, yawning, runny nose, sneezing, tears, aches, sweating or chills with goose bumps ("cold turkey"), diarrhoea, tremor, abdominal cramps, low blood pressure and involuntary leg movements. These symptoms are accompanied by a strong craving for the drug.

Withdrawal symptoms

• Major withdrawal symptoms peak between 48 and 72 hours after the last dose then gradually subside after a week. After-depression, stress, weakness, sleeplessness and drug craving can however, last for several weeks or months.

• *Heroin withdrawal is never fatal* to otherwise healthy adults, but sudden withdrawal by heavily dependent users who are in poor health can be fatal.





Treatment of opiate addiction

- Methadone maintenance: methadone 15-40 mg used as heroin substitute daily, coupled with gradual reduction of dose over several weeks/ months, until complete abstinence is achieved.
- Methadone-based programs substitute one addiction for another, enslaving patients to return day after day for their medication.
- Methadone has long-lasting effects and is one of the most difficult drugs to detox. from. Some methadone maintenance patients remain in these types of programs for 20-years.



Fentanyl abuse

• Fentanyl is a synthetic opiate with very powerful analgesic effects, used to prevent pain after surgery and other medical procedures. It is ~100 times more potent than morphine, has a more rapid onset of action and an effect of 1-2 hrs.

 It can be given i/v (during anaesthesia), orally (sublingual tablets/lozenges), intra-nasally, or as transdermal patches for chronic pain.



Fentanyl abuse

• Fentanyl is more deadlier than heroin! The photo below compares a lethal dose of heroin (~30 mg) with a lethal dose of fentanyl (~3 mg) and derivative carfentanil (~20 µg). It is so dangerous that even an accidental touch or breath of the powder can be fatal (police, forensic labs). It is believed that the singer *Prince* died from an accidental overdose of Fentanyl.



Fentanyl abuse

• Fentanyl abuse is now at crisis level in the USA and is rapidly becoming a problem also for drug abusers in the UK, since it is being mixed with street heroin to make it more potent. It is estimated that drug overdoses killed ~64,000 people in the USA in 2016, many of these deaths being blamed on fentanyl overdoses. In the UK, 60 deaths were linked to fentanyl abuse in 2017.





Cannabis



Cannabis sativa

*∆*⁹-*THC*

Cannabis plants





-Body high





Cannabis

- Cannabis, also known as Marijuana, Weed, Dope, Ganja, Wacky Backy, Hash, Hashish, Mary-Jane, Grass and Pot is currently the most common illicit drug used recreationally for its psychoactive euphoric effects - main active constituent is:
- Δ⁹-tetrahydrocannabinol (Δ⁹-THC) (Class B)
- Acts on specific cannabinoid CB₁ receptors



 Recently, strains of *Cannabis sativa* (*skunk*) with THC content up to 25% are becoming more popular, with stronger psychoactive effects and more serious possibility of harmful side-effects after prolonged use.

Effects of Cannabis

 Cannabis is usually smoked (with tobacco), or eaten (less effective). 'Normal' pricing tends to be ~£10-£12 (€10) for 1 g.



• Main short-term effects: Mood elevation ('high'), heightened-senses, relaxation, creative thinking, reduced nausea, increased appetite (*the 'munchies'*), tachycardia, pain relief, vasodilation, bronchodilation, dry mouth, hypothermia and short-term memory loss.

Chronic use→ cognitive impairment, anxiety, schizophrenia-symptoms, hallucinations, lung damage, depression, apathy, social withdrawal, possible suicide, cannabis use disorder (difficulty controlling cannabis use).

Cannabis dependence



• Mild psychological dependence to Cannabis may develop - mild physical dependence, and mild withdrawal effects:- craving, nausea, sweating, increased restlessness, irritability, mood changes, anger, depression, loss of appetite, insomnia. Cannabis has relatively *low* addiction potential.

• **Some mild tolerance** can develop with prolonged cannabis use.
Cannabis dependence



Cannabis use disorder (cannabis addiction) \rightarrow is the continued use of cannabis developing in ~10% of users, despite clinically significant distress or impairment which includes:

- a strong desire to take cannabis
- difficulties in controlling its use
- persisting in its use despite clinically harmful consequences
- a higher priority given to cannabis use than to other activities and obligations
- increased tolerance

• mild withdrawal state: \rightarrow anxiety, irritability, depression, restlessness, disturbed sleep, G/I symptoms, \downarrow appetite – symptoms mostly resolve after a few weeks.

Cannabis dependence



Cannabinoid hyperemesis syndrome

Cannabinoid hyperemesis syndrome (CHS) is a rare condition that causes repeated and severe bouts of vomiting and abdominal pain in some daily long-term users of marijuana. Apart from CNS effects, Δ^9 -THC can also affect the digestive tract, delaying stomach emptying. It also affects the oesophageal sphincter.

Curiously, affected people take a lot of long hot showers during the day to ease their nausea (possible hot temperature effect on the hypothalamus, controlling temperature regulation and vomiting). Symptoms subside within 1-2 days after stopping cannabis use.

Cannabis dependence



Symptoms of Cannabinoid Hyperemesis Syndrome

Nausea	Tendency to use extremely hot baths/ showers for relief	Stomach pain
(x x)		ils
Difficulty eating or keeping food down	Weight loss	Severe vomiting and/or diarrhea, sometimes for days or weeks
H		E-

Source: Annals of Internal Medicine, March 2019; Base & Clinical Pharmacology & Toxicology, January 2018; BMJ Journals Gut, October 2004

BUSINESS INSIDER



How do cannabinoids produce their effects?

Membrane pertubation hypothesis

Lipid bilayer expansion hypothesis of anesthetic effect



Before discovery of CB receptors in 1988, it was thought, that due to their high lipid solubility, CBs dissolved in neuronal cell membranes and 'perturbed' the membrane fluidity, therefore altering behaviour of ion channels involved in excitability; *c.f.* general anaesthetics.

Cannabinoid receptors



Endogenous cannabinoids: anandamide, 2-arachidonylglycerol (2-AG) and palmitoyl- ethanolamide also exist.

Cannabinoid receptors



CB₁ and CB₂ receptors couple with Gi/oα proteins to inhibit adenylyl cyclase, inhibit voltage-gated Ca²⁺ channels, activate K⁺ currents (GIRK), activate mitogen-activated protein kinase (MAPK), and influence Nitric Oxide (NO) signaling.

Cannabinoid receptors

CB1 receptors mainly localized in the brain (hippocampus, cerebellum and cerebrum) CB2 receptors mainly situated in the periphery (spleen, tonsillar and immune cells)





Medicinal use of Cannabis – still controversial: oral THC analogues nabilone and dronabinol (USA) currently used for the relief of:-

- Chemotherapy-induced nausea and vomiting
 resistant to conventional anti-emetics.
- Appetite stimulation in cases of severe weight loss in anorexia or patients with AIDS.
- Treatment of acute and chronic pain.





In Jan 2010, an extract of Cannabis - Nabixmols (Sativex) containing a 1:1 mixture of Δ^9 -THC and a non-psychoactive constituent cannabidiol (CBD) given as a sublingual spray, was licensed in the UK for treatment of MS, neuropathic and cancer related pain.

A single spray dose delivers **2.7 mg THC** and **2.5 mg CBD.** However, NICE do not consider this to be cost-effective and do not recommend it's use for MS treatment (£375 for 270 dose spray) (October 2014).



Cannabis and individual cannabinoids are also potentially useful in treating:-

- Pain symptoms of fibromyalgia (chronic pain).
- MS and spinal cord injury, including spasticity.
- Bladder dysfunction in MS.
- Menstrual cramps, morning sickness, labour pain.
- ↑Intraocular pressure in late-stage glaucoma.
- Asthma (bronchodilation).
- Drug-resistant epilepsy;(canabidiol: CBD).- Epidiolex
 Now approved by FDA (USA) for severe childhood epilepsy:
 Lennox-Gastaut and Dravet syndromes.
- •Breast, prostate and colorectal cancer.
- Alcohol and opiate addiction.
- Tics in Tourette Syndrome; Dyskinesia in PD.
- Alzheimer's and Huntington's Diseases.



After changes recently introduced by the Home Secretary, medicinal cannabis oil (**cannabidiol: CBD**) has now become available for therapeutic use on prescription in the UK from Nov 1st 2018.

"Herbal CBD (hemp oil)" is already available from Health Stores as a "food supplement" in the UK but must contain <0.05% THC, therefore cannot give you a high! These preparations have variable quality and doubtful health benefits.



Prescribable cannabis oil containing CBD is more concentrated allowing for stronger medicinal properties; it will be available only via a specialist hospital doctor primarily for treating drug-resistant nausea/vomiting (cancer chemotherapy), rare intractable epilepsy (Lennox-Gastaut and Dravet syndromes), and chronic pain/spasticity in MS sufferers. https://www.nhs.uk/conditions/medical-cannabis/

Recreational use of cannabis

The UK government has no current intention of legalising cannabis for recreational use even though it is now legal in Uruguay (SA), some USA states (Alaska, California, Colorado, Maine, Massachusetts, Michigan, Nevada, Oregon, Vermont, and Washington), and also more recently in Canada (June 2018) and New York (March 2021). In the UK, cannabis continues to be a class B drug and possession still carries an unlimited fine and up to 5 years in prison or both.



Recreational use of cannabis

From 1 April 2024, it will be legal for adults in Germany to possess 25 grams or less of cannabis in public, up to 50 grams of dried cannabis in private and grow up to three cannabis plants at home. Non-profit cannabis social clubs for adults are due to be legalised in Germany on 1 July 2024.







Hallucinogens

• Hallucinogens (psychedelics) -alter thought, perception and mood, without CNS stimulation or depression.

e.g. Lysergic acid diethylamide (LSD), Mescaline (from a Mexican Peyote cactus), and Psilocybin (from some poisonous "magic" mushrooms).



LSD

- LSD (Lysergic acid diethylamide: "acid") white odourless powder, taken orally – usually in form of paper blotter divided into ~¼" decorated squares ('tabs'), containing ~30-100 µg LSD. Price can be ~£10 (~€10) per 'tab'.
- Also: LSD liquid, gelatine sheets, tablets (microdots) or capsules (uncommon).









LSD





LSD blotter 'tabs'

LSD

Effects of LSD

- LSD alters perception by creating distortions of sight, sound, touch and smell vivid sensory hallucinations-*"tripping"*. LSD acts as a partial agonist on 5-HT_{2A} receptors in the prefrontal cortex, limbic system and brainstem and ultimately increases cortical glutamate levels.
- "Bad trips" can involve frightening images, extreme paranoid thoughts → serious accidents and suicides.
 "Flashbacks" can occur weeks,

months or even years later.



Effects of LSD

• Albert Hofmann a chemist at Sandoz Labs in 1943, intentionally ingested **250 µg of LSD** and within an hour was experiencing radical shifts in mental perception. • "... little by little I could begin to enjoy the unprecedented colors and plays of shapes that persisted behind my closed eyes. Kaleidoscopic, fantastic images surged in on me, alternating, variegated, opening and then closing themselves in circles and spirals, exploding in coloured fountains, rearranging and hybridizing themselves in constant flux..."



LSD dependence

- LSD does not cause physical dependence, but some psychological dependence can occur. It does not produce strong positive reinforcement like other drugs of abuse.
- Tolerance can develop rapidly after regular use and dissipate equally rapidly without physical withdrawal symptoms or craving.





Ketamine



- Ketamine: ("K, Kit Kat, Cat Valium") similar to PCP (phenylcyclidine)- produces 'dissociative' anesthesia catatonia (no talking or reacting), amnesia, analgesia; hallucinations and vivid dreams; emergence delirium. Price is ~£20-30/g. Is still used for general anaesthesia in humans under careful supervision - has serious abuse potential. It stimulates the cardiovascular system, therefore good for emergency patients in shock. Chronic abuse can cause irreversible bladder damage.
- Blocks NMDAR channels at the 'PCP site' in usedependent man channels.
 inhibits nAChRs and Na⁺
 Ketamine

Ketamine

Clinical uses

In small doses, ketamine has been used for the treatment of **neuropathic pain** and also for some **chronic pain syndromes**.

More recently, in sub-anaesthetic i/v doses, it has been found to exhibit **rapid-onset antidepressant effects** (within a few hours/days), therefore has been found useful in patients with treatment-resistant bipolar depression.

REVIEW ARTICLE

Administration of ketamine for unipolar and bipolar depression

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Ketamine

Clinical uses

Ketamine-related drug could be 'watershed' in treating depression: 'Rapid acting' **esketamine** was approved by the FDA to treat people who don't respond to traditional psychiatric drugs

A new drug *esketamine* (Spravato) related to ketamine, was recently approved by the US FDA for the rapid treatment of depression in people unresponsive to traditional antidepressants (*e.g.* SSRIs: Prozac). The effects would be felt within hours or days, not weeks like traditional depression treatments.

To avoid potential abuse, esketamine (nasal spray) will have to be administered in an approved clinic, and patients will be required to stay there for at least two hours, twice a week (with possible boosters), and not to drive until after a night of rest. **Cost is \$5,572 for month 1; \$1,699–\$2,244 thereafter)!**



5-MeO-DMT



A "new" psychedelic mind-altering drug is becoming popular in the USA – toad venom. It is a hallucinogenic like LSD, psilocybin and mescaline, but far more potent and quicker acting. The drug comes from a Colorado river toad, *Bufo alvarius*, which produces toxic venom containing **5-MeO-DMT** (5-methoxy-N,Nа dimethyltryptamine or O-methyl-bufotenin): an extremely potent natural psychedelic, \sim 4-6 times more powerful than **DMT** (dimethyltryptamine) contained in the Amazonian psychedelic brew Ayahuasca. The drug extracted from the toad's venom glands is dried into a dust then smoked; users experience an intense trip within 10-30 seconds, lasting ~30-60 minutes during which time, vision, and sound become distorted.





Bufo alvarius

5-MeO-DMT



The drug has long been ingested by licking the poisonous amphibian's back (the venom is toxic!) but is now more commonly consumed as a smokable "dust" (~50 mg/dose). The liquid is extracted by milking the toad's toxic venom glands and then dehydrating it into a crumbly dry paste. In the USA it is a Schedule 1 drug, carrying a 10-year prison sentence for possession. Users generally hire Shamans or "facilitators" to distribute the drug at parties (\$200 to \$500 a head).

Users describe a greater feeling of awareness, connection to "God" or rebirth and undergo an altered mood and perception, with some even making major life changes. Some believe 5-MeO-DMT can cure their depression, anxiety and post-traumatic stress disorder (PTSD); others can become immobile and unresponsive, with intense emotional reactions, euphoria, convulsions, and vomiting. Smoking Toad venom is therefore risky and potentially dangerous.

DMT

N, N-dimethyltryptamine (DMT) itself is also considered an endogenous hallucinogen, since there is evidence that it is synthesised and metabolised in the brain and peripheral tissues, and it has been suggested that it may have possible physiological and therapeutic roles, as well as being a putative neurotransmitter. Interestingly, raised levels of DMT in CSF and urine have been detected in some cases of schizophrenia, suggesting that it may be a neuroregulatory agent which is responsive to stress or emotional reactions. It has even been speculated that DMT may play a role in events such as mystical states and near-death experiences as well as natural dreams. See: Barker SA. (2018). N, N-Dimethyltryptamine (DMT), an Endogenous Hallucinogen: Past, Present, and Future Research to Determine Its Role and Function. Front Neurosci. 12:536.

> Ayahuasca brew







Psychomotor stimulants

- Psychomotor stimulants are sympathomimetics they increase cortical and physiological arousal and behavioural excitement.
- e.g. Cocaine, Amphetamine, MDMA (Ecstacy, E)



Cocaine



Coca leaves



Cocaine

- Cocaine ("coke") is extracted from the leaves of the shrub Erythroxylon coca that grows in Peru, Colombia and Bolivia.
- Cocaine (HCl) is a white powdery crystal- commonly "snorted" or given *i.v.* Freebase cocaine is called crack (makes "crackling" sound when smoked).
 Street prices vary from about £30-£40 (~€55) per gram







Snorting a 'line' of cocaine is a common mode of administration, but it damages the lining of the nose and makes it open to infection.

Cocaine

"More than £15 million worth of UK banknotes are being destroyed each year because they are so heavily contaminated with cocaine, heroin or ecstasy that they cannot be put back into circulation".

Source: *The Observer* Date: 10 November 2002



It is claimed (Jan 2010) that every British (paper) banknote in circulation is contaminated by cocaine within weeks of entering circulation, indicating the spread of cocaine use in the UK.

Cocaine

With the recent introduction of new polymer £5-£20 notes, drug users are complaining the thicker and stronger plastic notes have left them with cut noses after trying to snort cocaine. This is being referred to as "getting Winstoned", referring to Winston Churchill's image appearing on the plastic fivers.


Cocaine

Cocaine mechanism



Effects of cocaine

Effects of cocaine: euphoria, 个self-confidence, sociability, energy and alertness; increased sympathomimetic effects: tachycardia, arrhythmia, 个BP, pupil dilation, coronary spasm, 个respiration, 个 body temperature and local anaesthesia.

Main physiological effects of Crack cocaine



Cocaine dependence

- Cocaine can induce strong psychological dependence but no physiological dependence.
- Cocaine withdrawal symptoms are less intense that the withdrawal symptoms of other drugs like alcohol and heroin, nut nevertheless can produce intense depression, irritability, exhaustion, and craving for more drug. Some tolerance can develop.









Amphetamine tabs

Amphetamine

Amphetamine

• Amphetamine ("speed") is an indirectly acting sympathomimetic amine, - acts *presynaptically* to release stores of NA and DA from nerve endings.

• Amphetamine was originally developed as an appetite suppressant and to fight fatigue and increase alertness among servicemen - banned in 1959.

• **Dexamphetamine (***Dexedrine***)** - still used to treat narcolepsy and ADHD in adults and children (paradoxically!). Also, a mixture of **amphetamine** and **dexamphetamine (***Adderall***)** is used to treat the same conditions.



Amphetamine



Effects of amphetamine

- Amphetamine (sulphate)- taken orally, nasally, or i.v. not very effective if smoked (with tobacco). The powder sells at about £5-13 a gram.
- Effects: euphoria, ↑alertness, confidence and concentration, rapid talking, ↑stamina and physical energy, ↓appetite, tachycardia, sweating, ↑BP and respiratory rate, hallucinations, insomnia, aggressiveness, panic or paranoia ('amphetamine psychosis').



Amphetamine dependence

- Strong psychological dependence can develop but no clear cut physical dependence - mild withdrawal symptoms: lethargy, poor concentration, hunger, excessive sleep, intense craving for the drug.
- Tolerance develops rapidly to the euphoric and other physiological effects of amphetamine.



Methamphetamine





"Crystal meth"

Methamphetamine

Methamphetamine

- Methamphetamine ("meth", "ice", "crystal") is a very highly addictive stimulant related to amphetamine, with more longer lasting and toxic effects on the CNS. It sells at around £200/g.
- "Crystal meth" is a crystalline smokeable form of methamphetamine - becoming increasingly popular alongside alcohol and cannabis. 1 g of crystal meth can cost up to £260, compared with £30-40/g of cocaine, £5-13/g of amphetamine, and £10 for a 100 mg 'bag' of heroin.

MDMA (Ecstasy; E)



Ecstasy tablets



Ecstasy

- MDMA (Ecstasy; 'E', Adam, Beans, Biscuit, Clarity, Disco Biscuit, Eve, Go, Hug Drug, Lover's Speed, Peace, STP, X, XTC, Molly) – originally synthesized as an appetite suppressant - has both hallucinogenic and psychomotor stimulant amphetamine-like properties. It has a particular affinity for the 5-HT transporter (SERT).
- Ecstasy increases the activity of 5-HT and DA neurones in the brain. Now commonly used in dance clubs and all-night 'raves'.







Ecstasy



Effects of ecstasy

- Ecstasy is a Class A substance (UK), usually taken in the form of 100-200 mg tablets, which can also be crushed and snorted or injected. Average price is ~£5-15 per tablet.
- Ecstasy causes feelings of well-being, + connection with others (*empathogenic*). At high doses →severe anxiety, hallucinations, ↑HR, ↑BP, muscle cramps, teeth grinding, loss of consciousness or seizures. Also→ malignant hyperthermia, dehydration, liver, kidney, and CV system failure. Chronic use may damage 5HT neurones in the brain and interfere with memory function.

Ecstasy dependence

- Ecstasy- Psychological dependence and tolerance can develop, but not physical dependence.
- Withdrawal symptoms- these are mild and include: depression, anxiety, panic attacks, sleeplessness and paranoid delusions.



Ecstasy and serotonin syndrome

- Serotonin syndrome (SS) is a serious drug reaction, caused by medications that build up dangerously high levels of serotonin in the body- *e.g.*, SS may occur if you take an antidepressant with a migraine medication. Symptoms: mild (shivering and diarrhoea) to severe (muscle rigidity, arrhythmia, high fever and seizures)- fatal if not treated.
- SS can also occur in people exposed to MDMA, who have also taken one or more substances with serotonergic properties *e.g.*, amphetamines, cocaine, serotonin reuptake inhibitors (SSRIs) and opioids (some opioids- [tramadol, methadone]- inhibit the reuptake of serotonin by inhibiting SERT).

Ecstasy is still dangerous!

• Ecstasy is still a dangerous drug to experiment with-In March 2017, four schoolgirls aged 13, were taken to hospital after "taking pink teddy bear ecstasy pills" in Manchester. MDMA, is also now sold in powder form, and is at its purest in years, (sometimes >80%) purity): this means that pills sold nowadays can contain triple the typical dose found in the 80s or 90s. In 2021 there were 67 deaths linked to ecstasy in the UK; in 2022 there were 51.



Ecstasy is still dangerous!

• **Tusi (Pink cocaine)**- A new drug concoction called **tusi** has emerged in Latin America and in Europe and is now becoming popular in the US (~\$100/g) as a euphoriaproducing stimulant/hallucinogen. The concoction typically comes in the form of a nice smelling coloured pink powder containing MDMA mixed with ketamine, methamphetamine, opioids (fentanyl), caffeine, LSD and/or new designer psychoactive substances, 2C/2C-B. Snorting tusi is apparently quite painful; also taken as a pill, capsule or suppository! Can be extremely addictive/harmful- overdose can be fatal.



Kush

- Kush ("Zombie drug") is another new polydrug mixture creating serious problems in Sierra Leone (West Africa), where it is killing around a dozen people each week and hospitalising thousands. It is a mixture of cannabis, fentanyl, tramadol, formaldehyde and apparently, ground down human bones (provided by grave robbers?)!
- Kush costs around 20 UK pence per joint and is claimed to be highly addictive and often fatal, most likely due to its potent opioid content. The relevance of ground human bones, if true, is questionable. Users become sleepy, "spaced out", – disconnected from things happening around them, therefore more likely to be involved in serious accidents.



"Legal highs"

"Legal Highs" (now referred to as New Psychoactive **Substances:** NPS) are substances originally designed with stimulant or mood-altering properties to produce the same or similar effects to illegal drugs such as cocaine, ecstasy, cannabis or LSD. Up to May 2016, when the Psychoactive Substances Act 2016 came into effect, their sale or use was not banned by the current legislation regarding the misuse of drugs. Manufacturers therefore aimed to produce psychoactive substances that allowed them - and users – to evade the law, hence "Legal Highs".



26 May 2016

gal high





Psychoactive Substances Act 2016

The act applies across the UK and came into force on 26 May 2016. The act:

- makes it an offence to produce, supply, offer to supply, possess with intent to supply, possess on custodial premises, import or export psychoactive substances; that is, any substance intended for human consumption that is capable of producing a psychoactive effect. The maximum sentence will be 7 years' imprisonment.
- excludes legitimate substances, such as food, alcohol, tobacco, nicotine, caffeine and medical products from the scope of the offence, as well as controlled drugs, which continue to be regulated by the Misuse of

Drugs Act 1971.



- Stimulant-type drugs- mimic substances such as amphetamine, cocaine and ecstasy: mephedrone, BZP, MPDV, NRG-1, benzo Fury, Gogaine (3-FPM), MDAI and ethylphenidate.
- **Downers'/tranquiliser-type/sedative-type drugs** have inhibitory/relaxant effect on brain mimic benzodiazepines/alcohol/opiates: **etizolam, pyrazolam** and **flubromazepam, AH-7921.**
- Hallucinogenic drugs mimic substances like LSD-make users hallucinate, feel relaxed and happy or agitated and confused: 25i-NBOMe, bromo-dragonfly, BK-2CB, AMT, LSZ.

- Dissociative drugs mimic substances such as PCP (phencyclidine) and ketamine – cause detachment, hallucinations: Methoxetamine (MXE), 2-MDP, 8A-PHQ.
- Synthetic cannabinoids synthetic drugs that mimic Δ⁹-THC: Spice/K2, Clockwork Orange, Black Mamba, Annihilation, Mojo, Scooby Snax and Exodus Damnation.





Spice Gold/K2: one of the former "legal highs", once freely available on the internet and specialist 'head shops' is a herbal smoking mixture used as a Cannabis substitute – coated with synthetic cannabinoids, it is as powerful as some strains of strong 'skunk' cannabis – currently very popular with the prison population and rough sleepers – originally banned in the UK in December 2009. Now under the NPS Act 2016.

Cloud 9 vaping spice: "vaping" using an e-cigarette is now becoming a popular way to ingest a wide range of new synthetic drugs including synthetic cannabis sold as *Cloud 9, Hookah Relax, Crown, Bizzarro, Shisha and Mad Hatter.*









Mephedrone

Mephedrone: is a synthetic derivative of (-)cathinone found naturally in the E. African Khat plant; once sold legally as "plant food", originally banned in UK in April 2011. Now under the NPS Act 2016. Mephedrone ("meow-meow") produces euphoric, effects similar to cocaine, ecstasy, and methamphetamine – euphoria, stimulation, empathy. Several deaths have been related to mephedrone use.





MailOnline

High Street Highs:

October 2013. Matt, 17, almost died after buying 'legal high' drugs [*Exodus Damnation* –a herbal substance designed to be smoked like cannabis] from one of the new stores ("head Shops") that had opened up all over Britain, and police were powerless to act. Such shops are now banned under the Act.















So what can we legally buy now?

Now that dealing in *Legal Highs* has essentially been driven underground and on to the dark web, what can we still buy on the internet? The internet *Ice Head Shop* sells a variety of so-called energy pills and powders (containing **caffeine**!) as well as products claiming to contain CBD:













